

#33/dec.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: WALLACH=23

In re Application of:)	Conf. No. 2755
)	
David WALLACH et al)	Art Unit: 1635
)	
Appln. No.: 09/380,546)	Examiner: B. Whiteman
)	
Filed: November 29, 1999)	Washington, D.C.
)	
For: CASH (CASPASE HOMOLOGUE))	
WITH DEATH EFFECTOR DOMAIN,)	
MODULATORS OF THE FUNCTION)	
OF FAS RECEPTORS)	

DECLARATION UNDER 37 CFR §1.131

Honorable Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Yura "Yury" GOLTSEV, hereby declare and state as follows:

I am the same Yura Goltsev named as a co-inventor in the above-identified application and my educational and professional experience is presented in the curriculum vitae attached hereto as Exhibit A.

The experiments and computer searches described below were either conducted by me or under my supervision, and I can attest of my own personal knowledge that all the results reported herein and the dates ascribed thereto are true and accurate.

It is my understanding that the claims of the above-identified application remain rejected under 35 U.S.C. §102(e) as being anticipated by Shu et al., U.S. Patent No. 6,242,569. The filing date of U.S. Patent No. 6,242,569 for purposes of §102(e) is February 5, 1997.

The present declaration is intended to establish that the invention of the subject matter of the rejected claims was made on or before the effective filing date of U.S. Patent No. 6,242,569. The following shows conception on or before February 5, 1997, and diligence until the filing of Israeli patent application IL 120367, from which the benefit of foreign priority is claimed in the above-identified application, on March 3, 1997, as a constructive reduction to practice.

The dates of the experiments and computer searches to show conception are excised but every excised date is on or before February 5, 1997. Furthermore, the experiments and computer searches were done in Israel, a WTO member country, on or after January 1, 1996.

Attached hereto as Exhibit B are pages 106, 107 and 110 of my laboratory notebook (with the dates excised) with entries made by me in my own handwriting. Page 106 shows a two hybrid (2H) screen of MCH4L with a Jurkat library (in GAD1318 vector) without 3AA and restriction enzyme digests of

clones obtained from the Jurkat library. A continuation of the restriction enzyme digests of the clones from the Jurkat library is shown on page 107. The heading for page 110 is "Cloning of G1 isoforms", where the clones were obtained from RT-PCR of HeLa pA RNA. Restriction enzyme digestions of the clones are shown on page 110, where the "circled" clones were sequenced.

To clarify the terminology used for the polypeptide of the present invention, the G1 α isoform (long splice variant) of SEQ ID NO:2, encoded by the nucleotide sequence of SEQ ID NO:1, is also referred to as CASH α or CASHa, as will be seen in some Exhibits presented herein. Likewise, the G1 β isoform (short splice variant) of SEQ ID NO:4, encoded by the nucleotide sequence of SEQ ID NO:3, is also referred to as CASH β or CASHb.

Two nucleotide sequences, designated j13.1789 and j15.1789, obtained from the G1 isoform clones are shown in Exhibit C. These two nucleotide sequences overlap (but on different strands) to give the nucleotide sequence of the short variant G1 β isoform (CASH β or CASHb).

For purposes of showing the relationship of the sequences j13.1789 and j15.1789 to CASHb, a color schematic diagram, which is not intended to be to scale, is presented as Exhibit D, where each color represents regions of sequence

identity. The vertical lines starting from the left indicate the start of the coding sequence for CASHa and CASHb, the end of the region of similarity between CASHa and CASHb, the end (bSTOP) of the coding sequence of CASHb, and the end (aSTOP) of the coding sequence of CASHa. As can be seen from this schematic diagram, the nucleotide sequences of j13.1789 and j15.1789 cover the entire coding sequence of CASHb. The sequences labeled with accession numbers AA149562, AA151642, N94588, and W23795 are contigs identified for CASHa and CASHb that were available in the GenBank (NCBI) sequence database prior to the date the invention was made. The sequence database printouts for these contigs are presented as Exhibit E.

Part of the sequence from j15.1789 was used in a BLAST search for identification of similar protein coding regions in the GenBank database. The BLAST search results are presented as Exhibit F and the 313 base pair query sequence used in the BLAST search is shown in Exhibit G.

To search for other splice variants (which is routinely done in the art) of CASHb, a 219 base pair query sequence from j13.1789, shown as Exhibit H, was used in a BLAST search (Exhibit I) for identifying from the GenBank EST database, ESTs with nearly identical sequences. As shown in Exhibit I, the EST sequences with accession numbers AA149562

and AA15142 (highlighted) were identified. The yellow highlighting is not part of the original document and was made contemporaneously herewith to aid the examiner's understanding of this document. EST accession numbers AA149562 and AA151642 are the same accession numbers shown in Exhibit D to generate contigs for the coding sequence of CASHa. Accordingly, from the j15.1789 and j13.1789 sequences generated from the G1 isoform clones and the contigs identified based on BLAST sequence similarity searches, as summarized in Exhibit D, the nucleotide sequences and the encoded amino acid sequences for CASHa and CASHb were obtained, and therefore the present invention was conceived on or before February 5, 1997.

A printout from the "Sequencher" program dated February 8, 1997, supplemented with my hand made drawings on the printout, is attached hereto as Exhibit J. This printout is a contig of ESTs for CASHa and CASHb which lists more ESTs as well as contigs from The Institute for Genomics Research (TIGR) database that have regions coinciding with the CASH sequences.

As the sequences of both the short and long splice variants of CASH (CASHb and CASHa) were obtained by a combination of overlapping clones and contigs identified from a search of an EST sequences database, I set out to confirm the sequence for both CASHb and CASHa by ordering the

synthesis of oligonucleotide primers for use in sequencing/PCR. An ordering form with the heading "Oligos for G1" dated February 9, 1997, and showing the oligo primers ordered, with my handwriting on the side to indicate the identifying number for each the primers ordered, is attached hereto as Exhibit K.

Exhibit L is an updated version of Exhibit J. While it is undated, it was attached to the ordering form dated February 9, 1997, herein presented as Exhibit K. At the bottom of Exhibit L, I had noted in my own handwriting the approximate positions of the oligo primers, i.e., 18046, 18044, etc., first identified in Exhibit K.

Pages 111-113 from my laboratory notebook are attached hereto as Exhibit M, where page 111 shows an analysis of cDNA clones containing CASH sequences recovered from a library and page 112 shows restriction enzyme digests of plasmids containing cDNA fragments subcloned from the clones presented on page 111. While page 111 is undated, I performed this experiment either before or contemporaneously with the experiment on page 112. Page 113, also undated, shows a restriction enzyme analysis of plasmids expressing deletion mutants of CASH.

Attached hereto as Exhibit N is the printout from a BLAST search of the GenBank EST database using a 139 base pair

sequence from murine CASH as the query sequence. Note that on page 3 of this printout the BLAST search was conducted on February 16, 1997.

The sequences identified by 10609.1818, 11717.1818, and 18648.1818, dated February 25, 1997, and attached hereto as Exhibit O, are from sequencing a CASHb expression vector using three different primers, one of which (primer 18648) is shown on the oligo ordering form presented as Exhibit K.

Similarly, sequencing of a CASHa expression vector yielded the sequences identified by rti-651.1831 and rtl-648.1831, dated March 3, 1997, and attached hereto as Exhibit P.

The sequences of some "V" clones containing CASH (both long and short) obtained from cDNA library screening, dated February 25, 1997, are presented in Exhibit Q.

Exhibit R, attached hereto, presents three sheets that were attached together in my datafile. The first page is an undated schematic hand made drawing of V clones containing CASH (both long and short). The second page is a "Sequencher" contig, dated February 26, 1997, of ESTs and the sequences of some the V clones. The third page, dated February 27, 1997, is a more expanded contig including ESTs and the sequences for V clones.

In conclusion, the conception of the present invention occurred on or before February 5, 1997, and there was diligence from February 5, 1997, the date of filing of U.S. Patent No. 6,242,569, until the March 3, 1997, filing of Israeli patent application IL 120367 as a constructive reduction to practice. Accordingly, the applied Shu et al. reference, U.S. Patent No. 6,242,569, is antedated and withdrawal of the 35 U.S.C. §102(e) rejection is warranted.

The undersigned declares further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

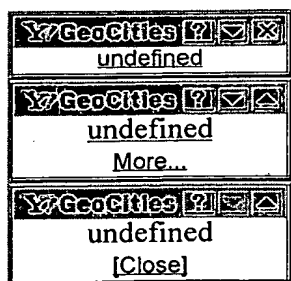
27 May 2003
Date


Yura Goltsev

09-380546

#33

Exhibit A



CURRICULUM VITAE

Yury V. Goltsev

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<http://www.geocities.com/bmyury/science>

EDUCATION:

1989-1993:	Bachelor of Science Moscow Institute for Physics and Technology Majors in Physical Chemistry and Biophysics
1993-1995:	Master of Science Moscow Institute for Physics and Technology Subject area: Molecular Biophysics
1995-2002:	Ph.D. in Molecular Biology The Weizmann Institute of Science Supervisor: Prof. David Wallach Thesis topic: Novel approaches to identification of signaling molecules activated by receptors of the TNF/NGF family, and their application to the study of cFLIP/CASH

DATE OF BIRTH: June 10th, 1972

MARITAL STATUS: married, two children

CITIZENSHIP: Israel

MY REFEREES ARE:

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AREA OF SCIENTIFIC EXPERTISE:

Last six years: Molecular analysis of cytokine-induced signal transduction pathways, in particular those triggered by the TNF/FAS-family members. Molecular regulation of apoptosis.

TECHNICAL SKILLS:

Recombinant DNA: conventional molecular cloning techniques, RT-PCR, site-directed mutagenesis, construction of cDNA libraries, DNA & RNA expression analysis (electrophoresis, hybridization, protection, etc), library screening, subtraction by Representation Difference Analysis (RDA)

Mammalian Cell Culture: routine, expression of recombinant protein in culture cells (both transient & stable), analysis: Western, Far Western, immunocytochemistry, GFP visualization system, essential flow cytometry and sorting, ELISA.

Signaling-related Techniques: EMSA & reporter assays for transcription, *in vitro* kinase assay (in gel & in solution), cell viability assays (biochemical and visual), *in vivo* labeling, *in vivo* signal transduction pathway reporting systems (e.g. PathFinder from Stratagene).

Protein-protein Interactions Assays: yeast two- and three-hybrid systems; mammalian interaction traps, *in vitro* pull-down, *in vivo* co-immunoprecipitation (both endogenous and transfected proteins).

Proteomics: Tandem Affinity Purification (TAP) of protein complexes and identification of the components by microsequencing.

Bacterial Expression: Introduction and affinity purification of recombinant proteins, essential HPLC (gel filtration, ion exchange)

PUBLICATIONS:

Boldin, M. P., Goncharov, T. M., Goltsev, Y. V., and Wallach, D. (1996). Involvement of MACH, a novel MORT1/FADD-interacting protease, in Fas/APO-1- and TNF receptor-induced cell death, *Cell* 85, 803-15.

Goltsev, Y. V., Kovalenko, A. V., Arnold, E., Varfolomeev, E. E., Brodianskii, V. M., and Wallach, D. (1997). CASH, a novel caspase homologue with death effector domains, *J Biol Chem* 272, 19641-4.

Wallach, D., Boldin, M., Goncharov, T., Goltsev, Y., Mett, I., Malinin, N., Adar, R., Kovalenko, A., and Varfolomeev, E. (1996). Exploring cell death mechanisms by analyzing signaling cascades of the TNF/NGF receptor family, *Behring Inst Mitt*, 144-55.

Wallach, D., Varfolomeev, E. E., Malinin, N. L., Goltsev, Y. V., Kovalenko, A. V., and Boldin, M. P. (1999). Tumor necrosis factor a receptor and Fas signaling mechanisms, *Annu Rev Immunol* 17, 331-67.

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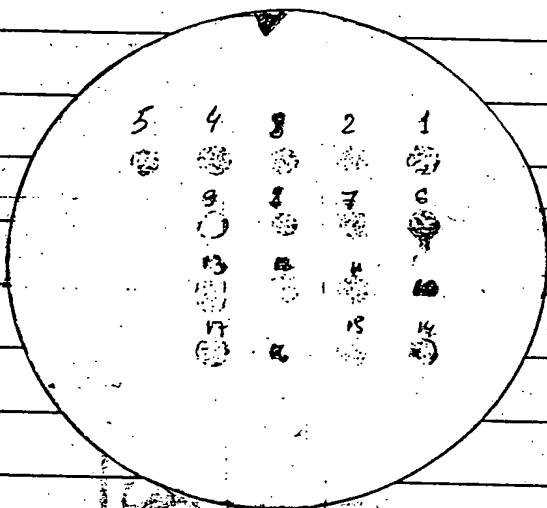
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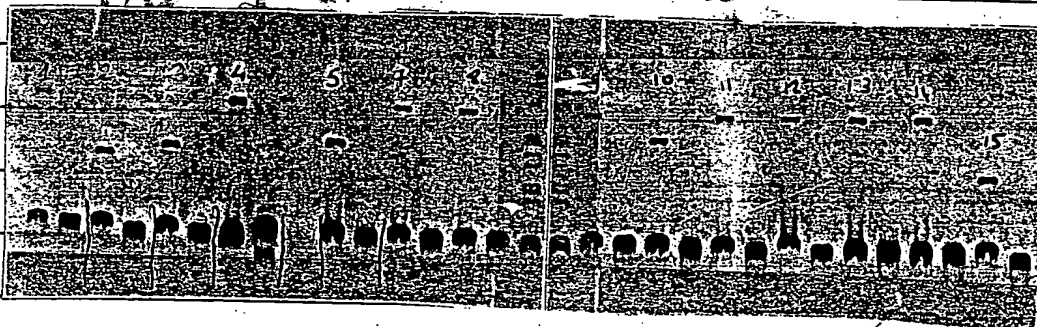
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 without 3AA Initial transform eff 200000 (without
 picked 1100 clones revival)

17 became blue in 1h Secondary testing of these 17

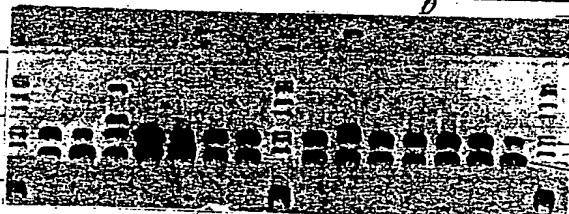


Restriction / Pst I

#9
 yeast 2



Resto / Not I + Bgl I



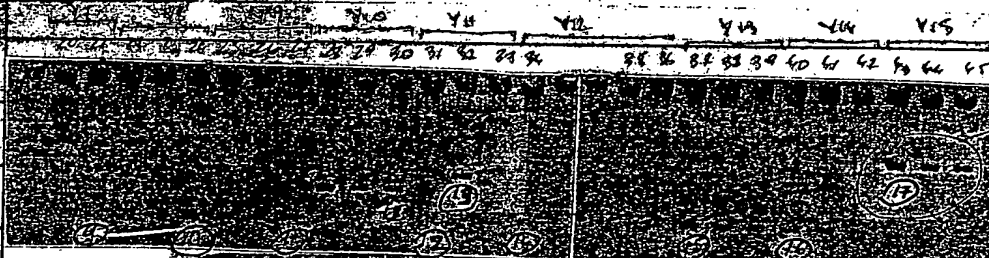
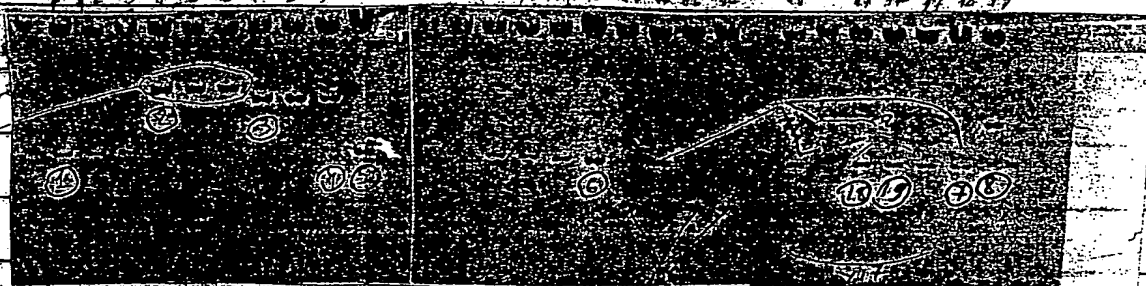
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DATE

Y1 Y2 Y3 Y4 Y5 Y6 Y7

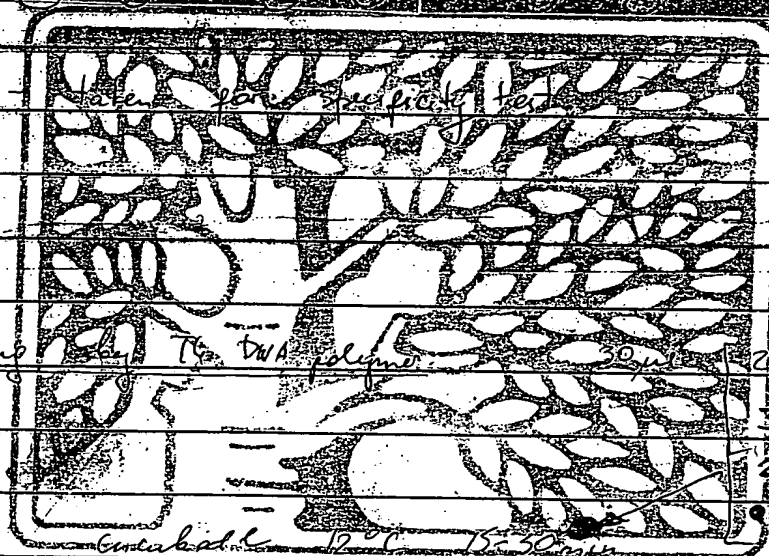
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MORE



MORE

①



Blunting Pvu II DNA polymerase 30 min 25 DNA + H₂O
 3 Lysen
 2 5mM dNTP
 0.5-1 T4
 incubate 12°C 15-30 min

Kinase (Phosphorylating) (from Red Protocol) Promega
 (for 30 μ l reaction) 10 μ mol adapters

50 mM Tris-HCl pH 7.5

10 mM MgCl₂

5 mM DTT

1-10 μ g dinucleotide

1 mM ATP

50 μ g/ml BSA

20 U T4 polynucleotide kinase

5 μ M ATP

37°C 1h

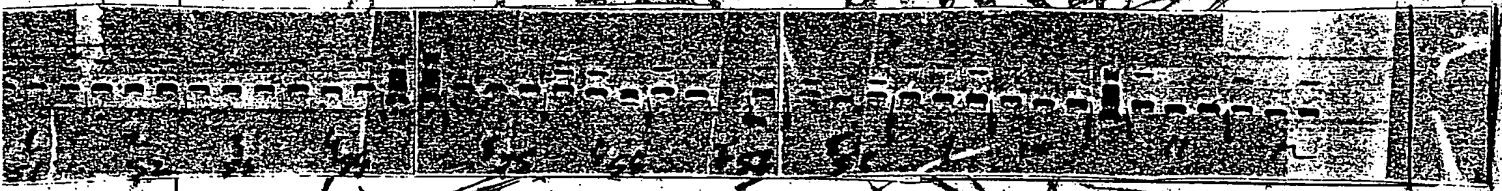
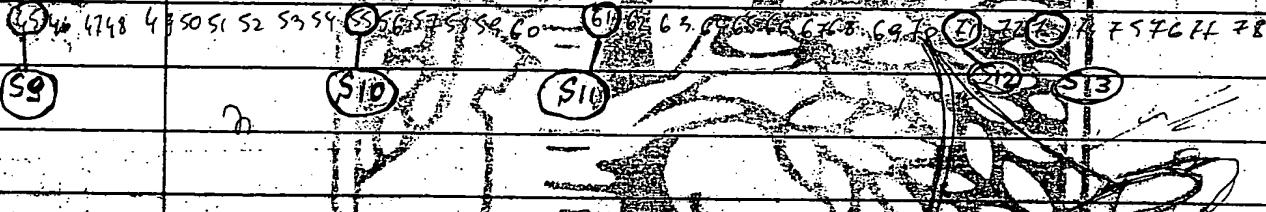
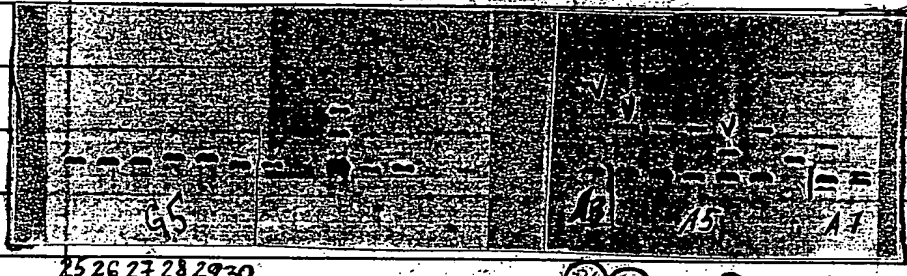
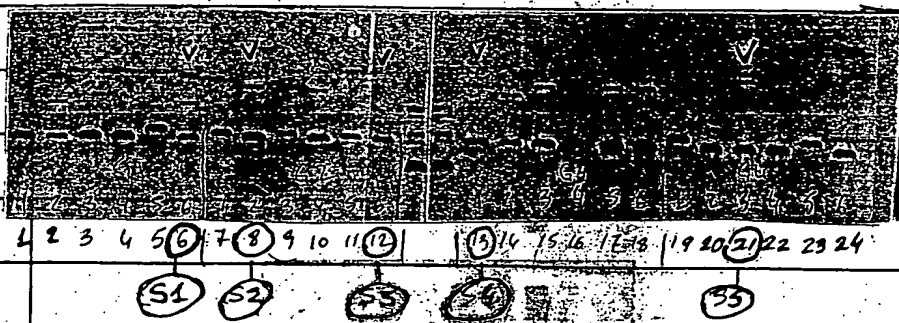
Maniatis

DATE

Cloning G1 isoforms / ET Xho

110

clones from
RT-PCR on
Hela pA RNA



~~Handwritten notes and diagrams, including a large 'X' and various scribbles.~~

~~Handwritten notes and diagrams, including a large 'X' and various scribbles.~~

ID: j13.1789 Your Ref: SampleB-1789 27
789.seq Leng: 929

Type: N Check: 3143 ..

1 CGATTCATAG ATCAGGGTTT TCCCAGTCAC GACGTTGTAA AACGACGGCC
51 AGTGGAATTG TAATACGACT CACTATAGGG CGAATTGGGT ACCGGGCCCC
101 CCCTCGAGGT CGAGCGGCCG CAGGGAATTT TTTTTTTTTT TTTTTTTTTT
151 TTTTTTTTTT AAAAAGTACA AGGGATATTT ATTTTATAGC ATTATTAGTA
201 gTAACAAAAG ATTGGAAAGC ATCTAAACAT ACAGCAACAA gAAAGGGCTa
251 aACACATTAT aACaCATTTA GAAAATGAAA CGATTTAATC aTTCCCAATG
301 ATAAANTTNA GGCATTCCAT NTTNNNCACA TGGAANAATT TCCANNCAAT
351 TTTCNTATCA TGACAGGGGG CTTNGGGTGT TNTCTNCCTN AANTTTTTTN
401 AAGGATCCTT NAAACTCTTT TGGATTGCTG CTTGGANAAA NTTCTGTAA
451 CTTGTCCCTG CNCCTATNAA NNGANTGCAG GGTACTTCTG GÄTTTTTGTC
501 TTCAGGTCTA TTCTGTGGAT GTTCTTTAGG CATTTTTCTA ATAAATCCCT
551 TGATCTGGGG CCCCCAATT ANTTCTCCC ACTCAACCAC AAGGTCCAAA
601 ~~AAACTCTTCT CCNNGCTTAT CTTGCCTCGG CCCCTGTTTC CTTCCTTGAN~~
651 GAAAATTATN ANGACNCTCC CATTTTCCNA NTCCTCCCCA TCTCTGCCAT
701 CACCCTCTAT TTCCNAAACA AGGTGANGGT TCTTACCAGG TGGGTTCN
751 CNCNTTCTN TCCTCTTCNA AANACTTTGA NCGGTCCNNT CCCCCCNNT
801 TAANATNCAC CANTCCCCAC CAAAAATTC TCTTTNCCNT CAATTCCAAA
851 GTCCNGNCTT AGGTGACCCA CTTTCCANCN CCGGCCNNA AANACNCCCC
901 CCCCNTTTA GTTCCCTCCC CTGAAGGTN

Exhibit C

your ID: j15.1789.) our Ref: SampleB-1789 22
j15.1789.seq Length: 928

Type: N Check: 7805 ..

1 CCCACCAAAC CAAAAAAGA GNCCTAGAAc TAGTCG~~ATG~~GGCAGAG
51 ~~GTGTCTGTG~~ AAGTCATCCA TCAGGTTGAA GAAGCACTTG ATACAGATGA
101 GAAGGAGATG CTGCTCTTTT TGTGCCGGA TGTGCTATA GATGTGGTTC
151 CACCTAATGT CAGGGGACCT TCTGGATATT TTACGGGAAA GAGGTAAGCT
201 GTCTGTCGGG GACTTGGCTG AACTGCTCTA CAGAGTGAGG CGATTTGACC
251 TGCTCAAACG TATCTTGAAG ATGGACAGAA AAGCTGTGGA GACCCACCTG
301 CTCAGGAACC CTCACCTTGT TTCGGACTAT AGAGTGCTGA TGGCAGAGAT
351 TGGTGAGGAT TTGGATAAAT CTGATGTGTC CTCaTTAATT TTCCTCNTGA
401 AGGATTACAT GGGCCGAGGC AaNATaATCA AGGAGAAgAN TTTCTTGAC
451 CTTGTGGTTG AATTGGGAgA AACTAAATCT GGTGCCCCN CNATCAACTG
501 GATTTATTAT AAAAATGCCT AAAGAACTCC CCCCANTANA CCTGAAGACA
551 AAAATCCANA ANTACTTCTN TCTGTNCNCG GANCANGGAC GANTTNCTNG
601 AATGTTCTCC TANCANCATC CNTNAGAATC TCCANGATCC TTCCNNTNAC
651 TTCNNGATGA TACCCCTNTC CCCNTGTCCT NATCTGAAAT TCTGGAAATT
701 GTCCATNTAA TTACNTGGAC TGCCTCNCNT TATCTTCNGN AACNAATAAA
751 TCTTCCCTNC CTAATGTTTT TNGAGNNTTT ACCCTCCCCG TTNCTGTTTN
801 TTANATCCTC CCCCCCCTG TTTCTCTNTT ATTCNNNNAA ANANTTCCCT
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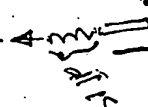
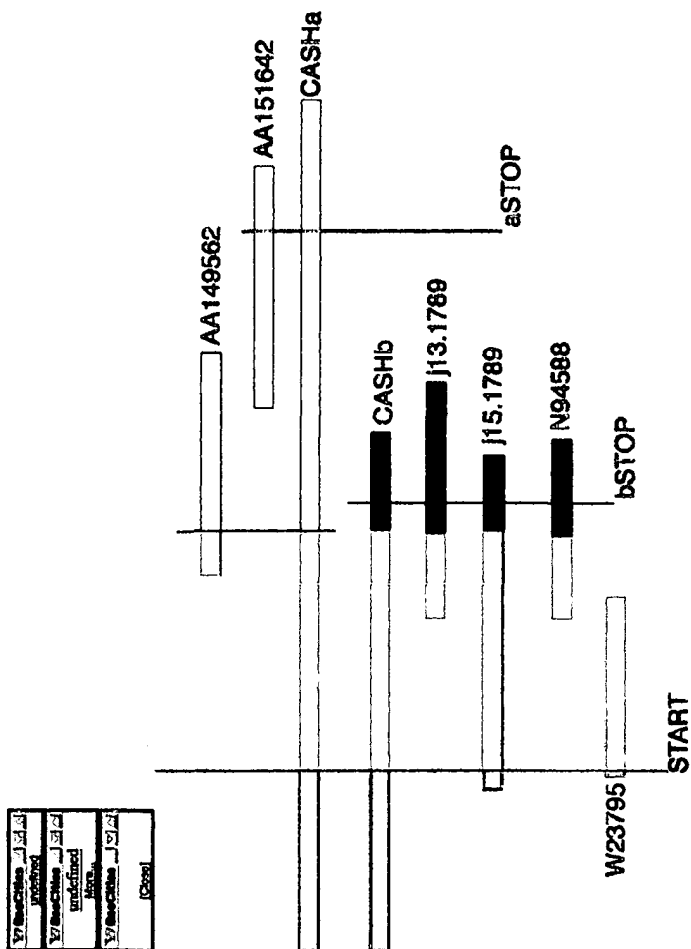
— 

Exhibit D



Address: 4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
Tel: 314 286 1800
Fax: 314 286 1810
E-mail: est@watson.wustl.edu

CITATIONS

Medline UID: [97044478](#)

Title: Generation and analysis of 280,000 human expressed sequence tags

Authors: Hillier, L., Lennon, G., Becker, M., Bonaldo, M.F., Chiapelli, B., Chissoe, S., Dietrich, N., DuBuque, T., Favello, A., Gish, W., Hawkins, M., Hultman, M., Kucaba, T., Lacy, M., Le, M., Le, N., Mardis, E., Moore, B., Morris, M., Parsons, J., Prange, C., Rifkin, L., Rohlfing, T., Schellenberg, K., Soares, M.B., Tan, F., Thierry-Mieg, J., Trevaskis, E., Underwood, K., Wohldmann, P., Waterston, R., Wilson, R., Marra, M.

Citation: Genome Res. 6 (9): 807-828 1996

MAP DATA

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Apr 28 2003 10:17:55



CGCTCAGGATAGGACTTCGCTAGGATCGGATCCCGGCGCTATTATATAGCTCGATCGATC
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CCCCATCT
CACAGACTCTACGCT

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Boo

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☐ 1: AA149562. zo29e05.r1 Strata...[gi:1720363]

Links

IDENTIFIERS

dbEST Id: 788753
EST name: zo29e05.r1
GenBank Acc: AA149562
GenBank gi: 1720363
GDB Id: 4620622

CLONE INFO

Clone Id: IMAGE:588320 (5')
Source: IMAGE Consortium, LLNL
DNA type: cDNA

PRIMERS

Sequencing: -28M13 rev2 from Amersham
PolyA Tail: Unknown

SEQUENCE

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GAGGATGTTTCATGGGAGAATCATGCCCTTATCTAGCAGGAAGCAAAGATGTTTTTATC

Quality: High quality sequence stops at base: 398

Entry Created: Dec 10 1996
Last Updated: Dec 10 1996

COMMENTS

This clone is available royalty-free through LLNL ; contact the IMAGE Consortium (info@image.llnl.gov) for further information.

LIBRARY

Lib Name: Stratagene colon (#937204)
Organism: Homo sapiens
Organ: colon
Tissue type: tumor
Cell line: T84 carcinoma cell line
Lab host: SOLR cells (kanamycin resistant)
Vector: pBluescript SK-
R. Site 1: EcoRI
R. Site 2: XhoI

Description: Cloned unidirectionally. Primer: Oligo dT. T-84 colonic epithelial cell line. Average insert size: 1.0 kb; Uni-ZAP XR Vector; ~5' adaptor sequence: 5' GAATTCGGCACGAG 3' ~3' adaptor sequence: 5' CTCGAGTTTTTTTTTTTTTTTTTTT 3'

SUBMITTER

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Institution: Washington University School of Medicine
Address: 4444 Forest Park Parkway, Box 8501, St. Louis, MO 63108
Tel: 314 286 1800
Fax: 314 286 1810
E-mail: est@watson.wustl.edu

CITATIONS

Medline UID: [97044478](#)
Title: Generation and analysis of 280,000 human expressed sequence tags
Authors: Hillier,L., Lennon,G., Becker,M., Bonaldo,M.F., Chiapelli,B., Chisoe,S., Dietrich,N., DuBuque,T., Favello,A., Gish,W., Hawkins,M., Hultman,M., Kucaba,T., Lacy,M., Le,M., Le,N., Mardis,E., Moore,B., Morris,M., Parsons,J., Prange,C., Rifkin,L., Rohlfing,T., Schellenberg,K., Soares,M.B., Tan,F., Thierry-Meg,J., Trevaskis,E., Underwood,K., Wohldmann,P., Waterston,R., Wilson,R., Marra,M.
Citation: Genome Res. 6 (9): 807-828 1996

MAP DATA

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Apr 28 2003 10:17:55



CGCTCAAGGATATTTATTTTATAGCATTATTAGTAGTAACAAAAGATTGGAAAGCATC
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PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Bio

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Show:

☐ 1: N94588. zb79a05.s1 Soares...[gi:1266897]

Links

IDENTIFIERS

dbEST Id: 501376
EST name: zb79a05.s1
GenBank Acc: N94588
GenBank gi: 1266897
GDB Id: 1253190

CLONE INFO

Clone Id: IMAGE:309776 (3')
Source: IMAGE Consortium, LLNL
Insert length: 939
DNA type: cDNA

PRIMERS

Sequencing: mob.REGA+ET
PolyA Tail: Unknown

SEQUENCE

GAAGTACAAGGATATTTATTTTATAGCATTATTAGTAGTAACAAAAGATTGGAAAGCATC
TAAACATACAGCAACAAGAAAGGGCTAAACACATTATAACACATTTAGAAAATGAAACGA
TTTAATCATTGAGATGATTAAGTAGAGGCAGTTCCATGTTAATCACATGGAACAATTTT
CAAGAATTTTTCAGATCAGGACAATGGGCATAGGGTGTTCATCCTGAAGTTATTTGAAG
GATCCTTGAGACTCTTTTGGATTGCTGCTTGGAGAACATTCCTGTAACCTGTCCCTGCTC
CTTTGAACAGACTGCTTGTACTTCTGGATTTTTGTCTTTTCAGGTCTATTCTGTGGATGTT
CTTTAGGCATTTTCTAATAAATCCAGTTGATCTGGGGCAACCAGATTTAGTTTCTCCAA
CTCAAC

Quality: High quality sequence stops at base: 292

Entry Created: May 9 1996
Last Updated: Aug 20 1996

COMMENTS

This clone is available royalty-free through LLNL ; contact the IMAGE Consortium (info@image.llnl.gov) for further information.

LIBRARY

Lib Name: Soares_senescent_fibroblasts_NbHSF
Organism: Homo sapiens
Tissue type: senescent fibroblast
Lab host: DH10B (ampicillin resistant)
Vector: pT7T3D (Pharmacia) with a modified polylinker V_TYPE:
phagemid
R. Site 1: Not I
R. Site 2: Eco RI
Description: 1st strand cDNA was primed with a Not I - oligo(dT) primer

[5' TGTTACCAATCTGAAGTGGGAGCGGCCGCATTTTTTTTTTTTTTTTTTTT 3'], double-stranded cDNA was size selected, ligated to Eco RI adapters (Pharmacia), digested with Not I and cloned into the Not I and Eco RI sites of a modified pT7T3 vector (Pharmacia). Library went through one round of normalization to a Cot = 5. Library constructed by Bento Soares and M.Fatima Bonaldo.

SUBMITTER

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Fax: 314 286 1810
E-mail: est@watson.wustl.edu

CITATIONS

Medline UID: [97044478](#)
Title: Generation and analysis of 280,000 human expressed sequence tags
Authors: Hillier,L., Lennon,G., Becker,M., Bonaldo,M.F., Chiapelli,B., Chissoe,S., Dietrich,N., DuBuque,T., Favello,A., Gish,W., Hawkins,M., Hultman,M., Kucaba,T., Lacy,M., Le,M., Le,N., Mardis,E., Moore,B., Morris,M., Parsons,J., Prange,C., Rifkin,L., Rohlfing,T., Schellenberg,K., Soares,M.B., Tan,F., Thierry-Meg,J., Trevaskis,E., Underwood,K., Wohldmann,P., Waterston,R., Wilson,R., Marra,M.
Citation: Genome Res. 6 (9): 807-828 1996

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Apr 28 2003 10:17:55

adapters (Pharmacia), digested with Not I and cloned into the Not I and Eco RI sites of a modified pT7T3 vector (Pharmacia). Library went through one round of normalization to a Cot = 5. Library constructed by Bento Soares and M.Fatima Bonaldo.

SUBMITTER

Name: Wilson RK
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CITATIONS

Medline UID: 97044478
Title: Generation and analysis of 280,000 human expressed sequence tags
Authors: Hillier,L., Lennon,G., Becker,M., Bonaldo,M.F., Chiapelli,B., Chissoe,S., Dietrich,N., DuBuque,T., Favello,A., Gish,W., Hawkins,M., Hultman,M., Kucaba,T., Lacy,M., Le,M., Le,N., Mardis,E., Moore,B., Morris,M., Parsons,J., Prange,C., Rifkin,L., Rohlfing,T., Schellenberg,K., Soares,M.B., Tan,F., Thierry-Meg,J., Trevaskis,E., Underwood,K., Wohldmann,P., Waterston,R., Wilson,R., Marra,M.
Citation: Genome Res. 6 (9): 807-828 1996

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BLAST Search Results with RepeatMasker filtering, Entrez and SRS links

BLAST search performed using the National Center for Biotechnology Information's BLAST WWW Server. Repeat reporting and filtering performed by RepeatMasker from U. Washington.

Links to Entrez and to the Sequence Retrieval System (SRS) provided by the Human Genome Center, Baylor College of Medicine:

- E** = Retrieve Entrez links (e.g., Medline abstracts, FASTA-formatted sequence reports).
R = Retrieve Entrez links to Related sequences (neighbors).
S = Retrieve SRS links (if present).

Reference: Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.
 Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol. 215:403-10.

Notice: statistical significance is estimated under the assumption that the equivalent of one entire reading frame in the query sequence codes for protein and that significant alignments will involve only coding reading frames.

Query= tmpseq_1
 (313 letters)

Translating both strands of query sequence in all 6 reading frames

Database: Non-redundant GenBank CDS
 translations+PDB+SwissProt+SPupdate+PIR
 241,922 sequences; 68,723,500 total letters.

Searching.....done

		Reading	High	Smallest		
		Frame	Score	Sum	Probability	N
Sequences producing High-scoring Segment Pairs:					P (N)	
gi11718327	(U75698) ORF K13 [Kaposi's sarcom...	+3	121	3.0e-09	1	
gi11492103	(U60315) MC160L [Molluscum contag...	+3	69	7.4e-06	2	
pir11S55668	hypothetical protein E8 - equine ...	+3	66	4.2e-05	2	
gi11492102	(U60315) MC159L [Molluscum contag...	+3	63	9.5e-05	2	
gi11813378	(D86547) still life type 1 [Droso...	-3	40	0.00040	4	
sp1P472111GALR_HUMAN	GALANIN RECEPTOR (GAL1-R) /gi1559...	+2	73	0.26	1	
gi1158271	(X12896) CTAP-III protein (AA 1-8...	+3	46	0.59	2	
gi1208127	(M88539) Col-CTAP-III (Leu21) smal...	+3	46	0.70	2	
gi11685110	(U58210) tetrahydrofolate dehydro...	-3	68	0.79	1	
gi11791038	(X84709) mediator of receptor ind...	+3	51	0.87	2	
pir11A56912	FADD protein - human /gi1809487 (...	+3	51	0.87	2	
gb11002001	Sequence 1 from Patent US 4897348...	+3	44	0.91	2	
gi1208159	(M11517) connective tissue activa...	+3	44	0.92	2	
sp1P223661MY88_MOUSE	MYELOID DIFFERENTIATION PRIMARY R...	+3	66	0.95	1	
gi1807578	(M19420) unknown protein [Germist...	+1	43	0.98	2	
sp1P294251TX26_PHONI	NEUROTOXIN TX2-6 /pir11S29216 neu...	+1	34	0.99	2	
sp1P027751PF4L_HUMAN	PLATELET BASIC PROTEIN PRECURSOR ...	+3	44	0.9998	2	

ERgi11718327 (U75698) ORF K13 [Kaposi's sarcoma-associated herpesvirus]

Length = 139

Plus Strand HSPs:

Score = 121 (55.7 bits), Expect = 3.0e-09, P = 3.0e-09
Identities = 31/97 (31%), Positives = 51/97 (52%), Frame = +3

Query: 18 EVIHQVEEALDTDEKEMLLFLCRDVAIDVVPNVRLDILRERGKLSVGDLAELLYRVR 197
EV+ +V L TD++E++LFL + L L+E G+L+ LAE L+R
Sbjct: 5 EVLCEVARKLGTDDREVVLFLNLFIPQPTLAQLIGALRALKEEGRLTFFLLAECLFRAG 64

Query: 198 RFDLLKRILKMDRKAVETHLLRNPHLVSDYRVLMSEI 308
R DLL+ +L +D + +E HL S Y++ + +
Sbjct: 65 RRDLLRDLHLDPFRLERHLAGTMSYFSPYQLTVLHV 101

ERgi11492103 (U60315) MC160L [Molluscum contagiosum virus subtype 1]

Length = 371

Plus Strand HSPs:

Score = 69 (31.7 bits), Expect = 7.4e-06, Sum P(2) = 7.4e-06
Identities = 17/39 (43%), Positives = 24/39 (61%), Frame = +3

Query: 123 DLLDILRERGKLSVGDLAELLYRVRFRFDLLKRILKMDRK 239
D L L+ R L++ +AELL +RRFD+LK M R+
Sbjct: 42 DALRALQRRRLTLSSMAELLCALRRFDVLKVRFGMTR 80

Score = 60 (27.6 bits), Expect = 7.4e-06, Sum P(2) = 7.4e-06
Identities = 12/17 (70%), Positives = 13/17 (76%), Frame = +3

Query: 45 LDTDEKEMLLFLCRDVA 95
LD E E+L FLCRDVA
Sbjct: 18 LDASEHEVLRFCLRDVA 34

Score = 32 (14.7 bits), Expect = 6.8, Sum P(2) = 1.0
Identities = 8/16 (50%), Positives = 10/16 (62%), Frame = +3

Query: 162 VGDLAELLYRVRFRFDL 209
V L LL+ V R+DL
Sbjct: 148 VSVLVTLHVCRYDL 163

ERpir11S55668 hypothetical protein E8 - equine herpesvirus 2 gi1695247

(U20824) ORF E8 [Equine herpesvirus 2]
Length = 171

Plus Strand HSPs:

Score = 66 (30.4 bits), Expect = 4.2e-05, Sum P(2) = 4.2e-05
Identities = 15/34 (44%), Positives = 20/34 (58%), Frame = +3

Query: 120 RDLLDILRERGLSVGDLAELLYRVRREFDLLKRI 221
RD L + LS + ELL+RV R DL++RI
Sbjct: 39 RDAFKFLSDYACLSAANQMELLFRVGRDLDIRRI 72

Score = 55 (25.3 bits), Expect = 4.2e-05, Sum P(2) = 4.2e-05
Identities = 10/17 (58%), Positives = 13/17 (76%), Frame = +3

Query: 42 ALDTDEKEMLLFLCRDV 92
+LD DE E L+LCRD+
Sbjct: 12 SLDEDETETYLYLCRDL 28



gi11492102 (U60315) MC159L [Molluscum contagiosum virus subtype 1]

Length = 241

Plus Strand HSPs:

Score = 63 (29.0 bits), Expect = 9.5e-05, Sum P(2) = 9.5e-05
Identities = 15/44 (34%), Positives = 25/44 (56%), Frame = +3

Query: 117 VRDLLDILRERGLSVGDLAELLYRVRREFDLLKRILKMDRKAVE 248
V L L ++ KL++ L E+LY ++R DLLK + ++ E
Sbjct: 42 VTQALCSLSQQRKLTALALVEMLYVLQRMDDLKSREGLSKEGAE 85

Score = 58 (26.7 bits), Expect = 9.5e-05, Sum P(2) = 9.5e-05
Identities = 12/28 (42%), Positives = 16/28 (57%), Frame = +3

Query: -12 SAEVIHQVEEALDTDEKEMLLFLCRDVA 95
S + + E LD+ E +LLFLC D A
Sbjct: 9 SLPFLRHLLEELDSHEDSLLLFLCHDAA 36



gi11813378 (D86547) still life type 1 [Drosophila melanogaster]

Length = 2064

Minus Strand HSPs:

Score = 40 (18.4 bits), Expect = 0.00040, Sum P(4) = 0.00040
Identities = 10/38 (26%), Positives = 17/38 (44%), Frame = -3

Query: 125 VPDIRWNHIYSNIPAQKEQHLLLIKICFFNLMDDFSR 12
+PD ++ +Y E+ L C + N M+ F R
Sbjct: 1127 MPDNAYSTVYL RDAMSVEEFLASACARRNLNPMEHFVR 1164

Score = 39 (17.9 bits), Expect = 0.00040, Sum P(4) = 0.00040
Identities = 5/11 (45%), Positives = 8/11 (72%), Frame = -3

Query: 299 HQHSIVRNKVR 267
HQH+++ N R
Sbjct: 370 HQHNVINNTR 380

Score = 35 (16.1 bits), Expect = 0.00040, Sum P(4) = 0.00040
Identities = 8/14 (57%), Positives = 10/14 (71%), Frame = -1

Query: 172 KSPTDSLPLSRKIS 131
+SP DSLP R+ S

Sbjct: 724 RSPWDSLPSLRQDS 737

Score = 33 (15.2 bits), Expect = 0.00040, Sum P(4) = 0.00040
Identities = 7/24 (29%), Positives = 11/24 (45%), Frame = -3

Query: 260 EQVGLHSFSVHLQDTFEQVKSPHS 189
E LH+F L + E + + S
Sbjct: 597 ESYSLHTFEALLSQSMENLANAKS 620

ER

sp|P47211|GALR_HUMAN GALANIN RECEPTOR (GAL1-R) gi|559048 (L34339)

galanin receptor [Homo sapiens] gi|1297338 (U53511) galanin
receptor [Homo sapiens]
Length = 349

Plus Strand HSPs:

Score = 73 (33.6 bits), Expect = 0.31, P = 0.26
Identities = 12/22 (54%), Positives = 15/22 (68%), Frame = +2

Query: 221 LEDGQKSCGDPPAQEPSPCFGL 286
L +G SC +PPA EP P FG+
Sbjct: 8 LSEGNASCPEPPAPEPGPLFGI 29

ER

gi|58271 (X12896) CTAP-III protein (AA 1-86) [Cloning vector ps29P]

Length = 86

Plus Strand HSPs:

Score = 46 (21.2 bits), Expect = 0.88, Sum P(2) = 0.59
Identities = 11/31 (35%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVVPNVRL 128
EE+LD+D L LC + P N++ L
Sbjct: 8 EESLSDLYAELRCLCIKTTSGIHPKNIQSL 38

Score = 42 (19.3 bits), Expect = 0.88, Sum P(2) = 0.59
Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA 259
L+DG+K C DP A
Sbjct: 56 LKGRKICLDPDA 68

ER

gi|208127 (M88539) Col-CTAP-III(Leu21) small fusion protein [Cloning

vector] gi|208129 (M88538) Col-CTAP-III(Leu21) small fusion protein
[Cloning vector] gi|209574 (M88536) connective tissue activating
peptide III [Cloning vector]
Length = 91

Plus Strand HSPs:

Score = 46 (21.2 bits), Expect = 1.2, Sum P(2) = 0.70

Identities = 11/31 (35%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVPPNVRDL 128

EE+LD+D L LC + P N++ L

Sbjct: 13 EESLSDSLYAE LRCLCIKTTSGIHPKNIQSL 43

Score = 42 (19.3 bits), Expect = 1.2, Sum P(2) = 0.70

Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA 259

L+DG+K C DP A

Sbjct: 61 LKDGRKICLDPDA 73

ER

gi|1685110 (U58210) tetrahydrofolate dehydrogenase/cyclohydrolase

[Streptococcus thermophilus]

Length = 284

Minus Strand HSPs:

Score = 68 (31.3 bits), Expect = 1.6, P = 0.79

Identities = 13/40 (32%), Positives = 25/40 (62%), Frame = -3

Query: 284 VRNKVRVPEQVGLHSFSVHLQDTFEQVKSPHSVEQFSQVP 165

VRNK R ++ G HS +V+L ++ + + +E+++Q P

Sbjct: 50 VRNKERAAKAGFHSKTVNLSESLSEEELIEVIEKYNQNP 89

ER

gi|791038 (X84709) mediator of receptor induced toxicity [Homo sapiens]

Length = 208

Plus Strand HSPs:

Score = 51 (23.5 bits), Expect = 2.1, Sum P(2) = 0.87

Identities = 14/47 (29%), Positives = 22/47 (46%), Frame = +3

Query: 171 LAELLYRVRRFDLLKRILKMDRKAVETHLLRNPHLVSDYRVLMSEIG 311

L ELL +RR DLL+R+ + A L + + V+ +G

Sbjct: 63 LRELLASLRRHDLRRVDDFEAGAAAGAAPGEEDLCAAFNVICDNVG 109

Score = 42 (19.3 bits), Expect = 2.1, Sum P(2) = 0.87

Identities = 8/21 (38%), Positives = 12/21 (57%), Frame = +3

Query: 21 VIHQVEEALDTDEKEMLLFLC 83

++H V +L + E L FLC

Sbjct: 7 LLHSVSSSLSSSELTELKFLC 27

ER

pir|A56912 FADD protein - human gi|809487 (U24231) FADD [Homo sapiens]

Length = 208

Plus Strand HSPs:

Score = 51 (23.5 bits), Expect = 2.1, Sum P(2) = 0.87

Identities = 14/47 (29%), Positives = 22/47 (46%), Frame = +3

Query: 171 LAELLYRVRFDLLKRIKMDRKAVETHLLRNPHLVSDYRVLMSEIG 311
L ELL +RR DLL+R+ + A L + + V+ +G
Sbjct: 63 LRELLASLRRHDLRLRVDDFEAGAAAGAAPGEEDLCAAFNVICDNVG 109

Score = 42 (19.3 bits), Expect = 2.1, Sum P(2) = 0.87
Identities = 8/21 (38%), Positives = 12/21 (57%), Frame = +3

Query: 21 VIHQVEEALDTDEKEMLLFLC 83
++H V +L + E L FLC
Sbjct: 7 LLHSVSSSLSSSELTELKFLC 27



gb|I002001 Sequence 1 from Patent US 4897348 gb|I101081 Sequence 1 from

Patent WO 8501067
Length = 90

Plus Strand HSPs:

Score = 44 (20.2 bits), Expect = 2.5, Sum P(2) = 0.91
Identities = 10/31 (32%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVPPNVRDL 128
EE+LD+D L +C + P N++ L
Sbjct: 12 EESLDSLDLYAELRCMCIKTTSGIH~~P~~KNIQSL 42

Score = 42 (19.3 bits), Expect = 2.5, Sum P(2) = 0.91
Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA 259
L+DG+K C DP A
Sbjct: 60 LKDGRKICLDPDA 72



gi|208159 (M11517) connective tissue activating peptide-III [Artificial gene]

Length = 91

Plus Strand HSPs:

Score = 44 (20.2 bits), Expect = 2.6, Sum P(2) = 0.92
Identities = 10/31 (32%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVPPNVRDL 128
EE+LD+D L +C + P N++ L
Sbjct: 13 EESLDSLDLYAELRCMCIKTTSGIH~~P~~KNIQSL 43

Score = 42 (19.3 bits), Expect = 2.6, Sum P(2) = 0.92
Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA-259
L+DG+K C DP A
Sbjct: 61 LKDGRKICLDPDA 73

ERsp|P22366|MY88_MOUSE MYELOID DIFFERENTIATION PRIMARY RESPONSE PROTEIN

MYD88 pir||S11226 MyD88 protein - mouse gi|53294 (X51397) MyD88
protein (AA 1-243) [Mus musculus]
Length = 243

Plus Strand HSPs:

Score = 66 (30.4 bits), Expect = 2.9, P = 0.95
Identities = 17/42 (40%), Positives = 23/42 (54%), Frame = +3

Query: 96 IDVVPNNVRDLLDILRERGLSVGDLAELLYRVRFDLLKRI 221
++ P R LLD + R SVG L ELL + R D+LK +
Sbjct: 11 LETRPDPTRSLDDAWQGRSGASVGRLELLALLDREDILKEL 52

ERgi|807578 (M19420) unknown protein [Germiston virus]

Length = 75

Plus Strand HSPs:

Score = 43 (19.8 bits), Expect = 3.9, Sum P(2) = 0.98
Identities = 5/12 (41%), Positives = 8/12 (66%), Frame = +1

Query: 226 RWTEKLWRPTCS 261
+WT+ WR C+
Sbjct: 42 KWTQNFWRRLCA 53

Score = 39 (17.9 bits), Expect = 3.9, Sum P(2) = 0.98
Identities = 9/22 (40%), Positives = 12/22 (54%), Frame = +1

Query: 142 GKEVSCLSGTWLNCS*GDLT 207
G++ +C S L CS E D T
Sbjct: 8 GQKSTCPSSQVLKCSLELS DST 29

ERsp|P29425|TX26_PHONEI NEUROTOXIN TX2-6 pir||S29216 neurotoxin Tx2 -

spider (Phoneutria nigriventer) gi|256377 neurotoxin Tx2-6
[Phoneutria nigriventer=Brazilian armed spiders, venom, Peptide, 48 aa]
Length = 48

Plus Strand HSPs:

Score = 34 (15.6 bits), Expect = 4.3, Sum P(2) = 0.99
Identities = 6/13 (46%), Positives = 8/13 (61%), Frame = +1

Query: 121 GTFWIFYGKEVSC 159
G FWI + K +C
Sbjct: 34 GYFWIAWYKLANC 46

Score = 33 (15.2 bits), Expect = 4.3, Sum P(2) = 0.99
Identities = 6/13 (46%), Positives = 6/13 (46%), Frame = +2

Query: 89 CCYRCGST*CGGP 127
CC G C GP
Sbjct: 16 CCGERGEVCVGGP 28

ER

sp|P02775|PF4L_HUMAN_PLATELET BASIC PROTEIN PRECURSOR (PBP) (CONTAINS:

CONNECTIVE-TISSUE ACTIVATING PEPTIDE III (CTAP-III), LOW-AFFINITY
PLATELET FACTOR IV (LA-PF4), BETA-THROMBOGLOBULIN (BETA-TG),
NEUTROPHIL-ACTIVATING PEPTIDE 2 (NAP-2)) pir||TGHU
beta-thromboglobulin precursor - human gi|181176 (M54995)
connective tissue activating peptide III [Homo sapiens] gi|344294
(A01319) novel factor having neutrophil-stimulating activity
[unidentified]
Length = 128

Plus Strand HSPs:

Score = 44 (20.2 bits), Expect = 8.5, Sum P(2) = 1.0
Identities = 10/31 (32%), Positives = 16/31 (51%), Frame = +3

Query: 36 EEALDTDEKEMLLFLCRDVAIDVVPNVRL 128
EE+LD+D L +C + P N++ L
Sbjct: 50 EESLSDLYAELRCMCIKTTSGIHPKNIQSL 80

Score = 42 (19.3 bits), Expect = 8.5, Sum P(2) = 1.0
Identities = 8/13 (61%), Positives = 10/13 (76%), Frame = +2

Query: 221 LEDGQKSCGDPPA 259
L+DG+K C DP A
Sbjct: 98 LKDGRKICLDPDA 110

Parameters:

V=50

B=50

H=9

-filter=SEG

P=4

-ctxfactor=5.61

E=10

Query	Frame	MatID	Matrix name	----- Lambda	As Used K	----- H	----- Computed Lambda	K	----- H
Std.	0	0	BLOSUM62				0.319	0.135	0.396
+3	0	0	BLOSUM62	0.319	0.135	0.396	0.320	0.140	0.377
+2	0	0	BLOSUM62	0.319	0.135	0.396	0.376	0.173	0.727
+1	0	0	BLOSUM62	0.319	0.135	0.396	0.353	0.151	0.594
-1	0	0	BLOSUM62	0.319	0.135	0.396	0.335	0.143	0.410
-2	0	0	BLOSUM62	0.319	0.135	0.396	0.350	0.154	0.532
-3	0	0	BLOSUM62	0.319	0.135	0.396	0.334	0.143	0.458

Query	Frame	MatID	Length	Eff.Length	E	S	W	T	X	E2	S2
+3	0	0	103	103	10.	58	3	13	22	0.11	32
+2	0	0	104	104	10.	58	3	13	22	0.11	32
+1	0	0	104	104	10.	58	3	13	22	0.11	32
-1	0	0	104	65	10.	55	3	13	22	0.11	30
-2	0	0	104	104	10.	58	3	13	22	0.11	32
-3	0	0	103	103	10.	58	3	13	22	0.11	32

Statistics:

Query	Expected	Observed	HSPs	HSPs
Frame	MatID	High Score	High Score	Reportable Reported
+3	0	62 (28.5 bits)	121 (55.7 bits)	18 18
+2	0	62 (28.5 bits)	73 (33.6 bits)	7 7
+1	0	62 (28.5 bits)	62 (28.5 bits)	3 3
-1	0	58 (26.7 bits)	50 (23.0 bits)	1 1
-2	0	62 (28.5 bits)	59 (27.1 bits)	0 0
-3	0	62 (28.5 bits)	68 (31.3 bits)	4 4

Query	Neighborhood	Word	Excluded	Failed	Successful	Overlaps
Frame	MatID	Words	Hits	Extensions	Extensions	Excluded
+3	0	474	3643889	411910	3212799	19180 7
+2	0	1018	4815505	897825	3908333	9347 34
+1	0	1582	5097249	987386	4099341	10522 8
-1	0	287	1981913	251753	1723979	6181 6
-2	0	656	4186873	555161	3623591	8121 3
-3	0	947	4154885	590204	3549776	14905 7

Database: Non-redundant GenBank CDS translations+PDB+SwissProt+SPupdate+PIR

Release date:

Posted date: 8:09 AM EST

of letters in database: 68,723,500

of sequences in database: 241,922

of database sequences satisfying E: 17

No. of states in DFA: 571 (56 KB)

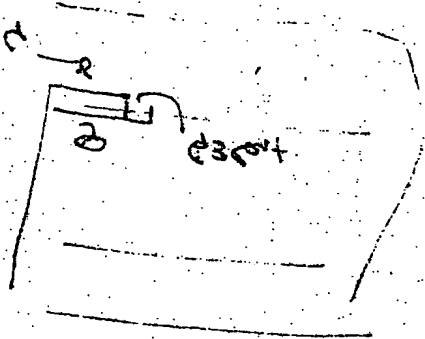
Total size of DFA: 109 KB (128 KB)

Time to generate neighborhood: 0.01u 0.01s 0.02t Real: 00:00:00

No. of processors used: 4

Time to search database: 47.57u 0.34s 47.91t Real: 00:00:12

Total cpu time: 47.64u 0.45s 48.09t Real: 00:00:12



DNA Strider™ 1.2

Exhibit G

mnest -> List

DNA sequence 313 b.p. agagtaggatgt ... agagattggtga linear

	10	20	30	40	50	60	
1	agagtaggat	gtctgctgaa	gtcatccatc	aggttgaaga	agcacttgat	acagatgaga	60
61	aggagatgct	gctctttttg	tgccgggatg	ttgctataga	tgtggttcca	cctaattgca	120
121	gggaccttct	ggatatttta	cgggaaagag	gttagctgtc	tgtcggggac	ttggctgaac	180
181	tgtctacag	agtgaggcga	tttgacctgc	tcaaacgtat	cttgaagatg	gacagaaaag	240
241	ctgtggagac	ccacctgctc	aggaaccctc	accttgtttc	ggactataga	gtgctgatgt	300
301	cagagattgg	tga					313
	10	20	30	40	50	60	

Exhibit H

>tmpseq1

GTGTGTGTCCTGGTGAGCCGAGGATCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTC
CCTGCATCACATCA

GGAGGATGTTTCATGGGAGATTCATGCCCTTATCTAGCAGGGAAGCCAAAGATGTTTTTATTCAGAACT
ATGTGGTGTGAG

AGGGCCAGCTGGAGGACAGCAGCCTCTTTGGAGGTGGATGGGGCCAGCGATGAAGAATG

Exhibit I

[Image]

[progress meter]

Search in progress, please wait for results

BLASTN 1.4.9MP [26-March-1996] [Build 14:27:07 Apr 1 1996]

Reference: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol. 215:403-10.

Notice: this program and its default parameter settings are optimized to find nearly identical sequences rapidly. To identify weak similarities encoded in nucleic acid, use BLASTX, TBLASTN or TBLASTX.

Query= tmpseq_1
(219 letters)

Database: Non-redundant Database of GenBank EST Division
816,369 sequences; 299,962,672 total letters.

Sequences producing High-scoring Segment Pairs:	High Score	Smallest Sum Probability P(N)	N
gb AA001257 AA001257 zh82c06.r1 Soares fetal liver spleen...	360	1.2e-63	3
dbj C05730 C05730 similar to none	250	4.5e-37	3
gb AA149562 AA149562 zo29e05.r1 Stratagene colon (#937204...	267	2.1e-33	3
gb T93307 T93307 ye29c04.s1 Homo sapiens cDNA clone 1...	191	2.4e-09	2
gb AA151642 AA151642 zo29e05.s1 Stratagene colon (#937204...	204	2.0e-07	1

gb|AA001257|AA001257 zh82c06.r1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 427786 5'.
Length = 615

Plus Strand HSPs:

Score = 360 (99.5 bits), Expect = 1.2e-63, Sum P(3) = 1.2e-63
Identities = 72/72 (100%), Positives = 72/72 (100%), Strand = Plus / Plus

Query: 135 TTTTATTCAGAACTATGTGGTGTTCAGAGGGCCAGCTGGAGGACAGCAGCCTCTTTGGAGG 194
|||||

Sbjct: 529 TTTTATTCAGAACTATGTGGTGTTCAGAGGGCCAGCTGGAGGACAGCAGCCTCTTTGGAGG 588

Query: 195 TGGATGGGGCCA 206
|||||

Sbjct: 589 TGGATGGGGCCA 600

Score = 353 (97.5 bits), Expect = 1.2e-63, Sum P(3) = 1.2e-63
Identities = 71/72 (98%), Positives = 71/72 (98%), Strand = Plus / Plus

Query: 67 CCTGCATCACATCAGGAGGATGTTTCATGGGAGATTCATGCCCTTATCTAGCAGGGAAGCC 126
|||||

Sbjct: 460 CCTGCATCACATCAGGAGGATGTTTCATGGGAGATTCATGCCCTTATCTAGCAGGGAAGCC 519

Query: 127 AAAGATGTTTTT 138
 ||||| |||
 Sbjct: 520 AAAGATGTNTTT 531

Score = 213 (58.9 bits), Expect = 1.2e-63, Sum P(3) = 1.2e-63
 Identities = 43/44 (97%), Positives = 43/44 (97%), Strand = Plus / Plus

Query: 25 TCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 68
 |||||
 Sbjct: 417 TCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCNC 460

Score = 139 (38.4 bits), Expect = 2.2e-57, Sum P(3) = 2.2e-57
 Identities = 35/45 (77%), Positives = 35/45 (77%), Strand = Plus / Plus

Query: 1 GTGTGTGTCCTGGTGAGCCGAGGATCCCAGAGTGTGTATGGTGTG 45
 |||||
 Sbjct: 391 GTGTGTGTCCTGGTGAGCCGAGGANNTCCCAGAGTGTGTATGGTG 435

dbj|C05730|C05730 similar to none
 Length = 521

Plus Strand HSPs:

Score = 250 (69.1 bits), Expect = 4.5e-37, Sum P(3) = 4.5e-37
 Identities = 52/55 (94%), Positives = 52/55 (94%), Strand = Plus / Plus

Query: 64 CTCCCTGCATCACATCAGGAGGATGTTTCATGGGAGATTCATGCCCTTATCTAGCA 118
 |
 Sbjct: 467 CCCCCTGCATCACATCAGGAAGATGTTTCNTGGGAGATTCATGCCCTTATCTAGCA 521

Score = 236 (65.2 bits), Expect = 4.5e-37, Sum P(3) = 4.5e-37
 Identities = 48/49 (97%), Positives = 48/49 (97%), Strand = Plus / Plus

Query: 20 GAGGATCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 68
 ||||
 Sbjct: 421 GAGGCTCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 469

Score = 120 (33.2 bits), Expect = 4.5e-37, Sum P(3) = 4.5e-37
 Identities = 24/24 (100%), Positives = 24/24 (100%), Strand = Plus / Plus

Query: 1 GTGTGTGTCCTGGTGAGCCGAGGA 24
 |||||
 Sbjct: 399 GTGTGTGTCCTGGTGAGCCGAGGA 422

gb|AA149562|AA149562 zo29e05.r1 Stratagene colon (#937204) Homo sapiens
 cDNA clone 588320 5'
 Length = 538

Plus Strand HSPs:

Score = 267 (73.8 bits), Expect = 2.1e-33, Sum P(3) = 2.1e-33
 Identities = 55/57 (96%), Positives = 55/57 (96%), Strand = Plus / Plus

Query: 66 CCCTGCATCACATCAGGAGGATGTTTCATGGGAGATTCATGCCCTTATCTAGCAGGGA 122
 |||
 Sbjct: 465 CCCTGCATCACATCAGGAGGATGTTTCATGGGAGAATCATGCCCTTATCTAGCAGGAA 521

Score = 221 (61.1 bits), Expect = 2.1e-33, Sum P(3) = 2.1e-33
 Identities = 45/46 (97%), Positives = 45/46 (97%), Strand = Plus / Plus

Query: 23 GATCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 68
 |
 Sbjct: 421 GGTCCCAGAGTGTGTATGGTGTGGATCAGACTCACTCAGGGCTCCC 466

Score = 135 (37.3 bits), Expect = 1.2e-24, Sum P(3) = 1.2e-24
 Identities = 35/45 (77%), Positives = 35/45 (77%), Strand = Plus / Plus

Query: 1 GTGTGTGTCCTGGTGAGCCGAGGATCCCAGAGTGTGTATGGTGTG 45
 |||
 Sbjct: 397 GTGTGTGTCCTGGTGAGCCGAGGAGGTCCCAGAGTGTGTATGGTGTG 441

Score = 75 (20.7 bits), Expect = 2.1e-33, Sum P(3) = 2.1e-33
 Identities = 15/15 (100%), Positives = 15/15 (100%), Strand = Plus / Plus

Query: 126 CAAAGATGTTTTTAT 140
 |||
 Sbjct: 523 CAAAGATGTTTTTAT 537

gb|T93307|T93307 ye29c04.s1 Homo sapiens cDNA clone 119142 3'.
 Length = 294

Minus Strand HSPs:

Score = 191 (52.8 bits), Expect = 2.4e-09, Sum P(2) = 2.4e-09
 Identities = 39/40 (97%), Positives = 39/40 (97%), Strand = Minus / Plus

Query: 190 CAAAGAGGCTGCTGTCCTCCAGCTGGCCCTCTGACACCAC 151
 |
 Sbjct: 255 CCAAGAGGCTGCTGTCCTCCAGCTGGCCCTCTGACACCAC 294

Score = 89 (24.6 bits), Expect = 2.4e-09, Sum P(2) = 2.4e-09
 Identities = 21/25 (84%), Positives = 21/25 (84%), Strand = Minus / Plus

Query: 212 TTATCGTGGCCCCATCCACCTCCAA 188
 |
 Sbjct: 234 TCATCGCTGGCCCCATCCACCTCCAA 258

gb|AA151642|AA151642 zo29e05.s1 Stratagene colon (#937204) Homo sapiens
 cDNA clone 588320 3' similar to contains Alu repetitive element;
 Length = 608

Minus Strand HSPs:

Score = 204 (56.4 bits), Expect = 2.0e-07, P = 2.0e-07
 Identities = 64/93 (68%), Positives = 64/93 (68%), Strand = Minus / Plus

Query: 187 AGAGGCTGCTGTCCTCCAGCTGGCCCTCTGACACCACATAGTTCTGAATAAAAAACATCTT 128
 |||||
 Sbjct: 446 AGAGGCTGCTGTCTCAAGCTGGGCCCTCTGACACCACATAGTTCTGAATAAAAAACATCT 505
 Query: 127 TGGCTTCCCTGCTAGATAAGGGCATGAATCTCC 95
 || ||
 Sbjct: 506 TTGGCTTCCCTGCTAGATAAGGGCTGAATCTCC 538

Parameters:

V=100
 B=50
 H=0
 P=4

-ctxfactor=2.00
 E=10

Query	Strand	MatID	Matrix name	----- Lambda	As Used K	----- H	----- Lambda	Computed K	----- H
+1	0	+5,-4	0.192	0.173	0.357	same	same	same	
-1	0	+5,-4	0.192	0.173	0.357	same	same	same	

Query	Strand	MatID	Length	Eff.Length	E	S	W	T	X	E2	S2
+1	0	219	219	10.	111	11	0	73	0.021	74	
-1	0	219	219	10.	111	11	0	73	0.021	74	

Statistics:

Query	Strand	MatID	Expected High Score	Observed High Score	HSPs Reportable	HSPs Reported
+1	0	119 (32.9 bits)	365 (100.9 bits)	11	11	
-1	0	119 (32.9 bits)	204 (56.4 bits)	3	3	

Query	Strand	MatID	Neighborhd Words	Word Hits	Excluded Hits	Failed Extensions	Successful Extensions	Overlaps Excluded
+1	0	212	26331	2286	22832	1213	1	
-1	0	212	23923	2040	20821	1062	5	

Database: Non-redundant Database of GenBank EST Division

Release date:

Posted date:

of letters in database: 299,962,672

of sequences in database: 816,369

of database sequences satisfying E: 5

No. of states in DFA: 172 (172 KB)

Total size of DFA: 178 KB (192 KB)

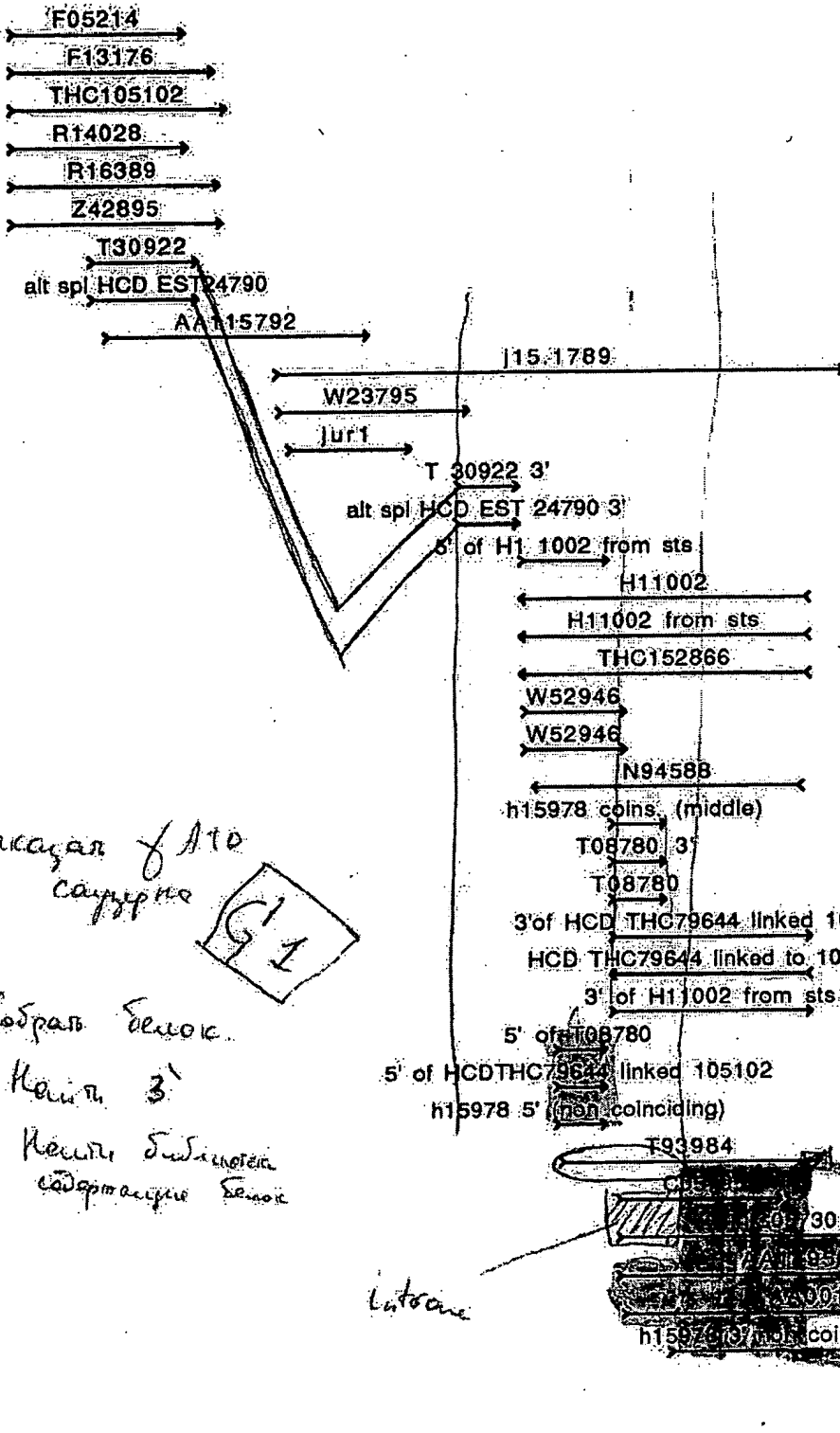
Time to generate neighborhood: 0.00u 0.00s 0.00t Real: 00:00:00

No. of processors used: 4

Time to search database: 9.20u 0.31s 9.51t Real: 00:00:03

Total cpu time: 9.21u 0.32s 9.53t Real: 00:00:03

Exhibit J



- Заканая 8110
для саппорта
1. Собран Белок.
2. Контин 3'
4. Контин 5' Белок
содержащий Белок

Exhibit K

Oligos for G1

2-9-1997

for 5' utr sense

5' GTT TCT TTG CCT CCA TCT TGG GTG CGC CTT 3' 18646

for atg in mm sense

5' ATG TCT GCT GAA GTC ATC CAT CAG GTT GAA 3' 18647

for before middle reg sense

5' CTG GTT GCC CCA GAT CAA CTG GAT TTA TTA 3' 18648

after middle antisense

5' GCC AAG CTG TTC CTT AAG TCT TTG TTC TTT 3' 18649

first strong homology in prot reg (YKMKS) sense

5' ACC TGA AGA GAG ATA CAA GAT GAA GAG CAA 3' 18650

for second subunit for (EADF) antisense

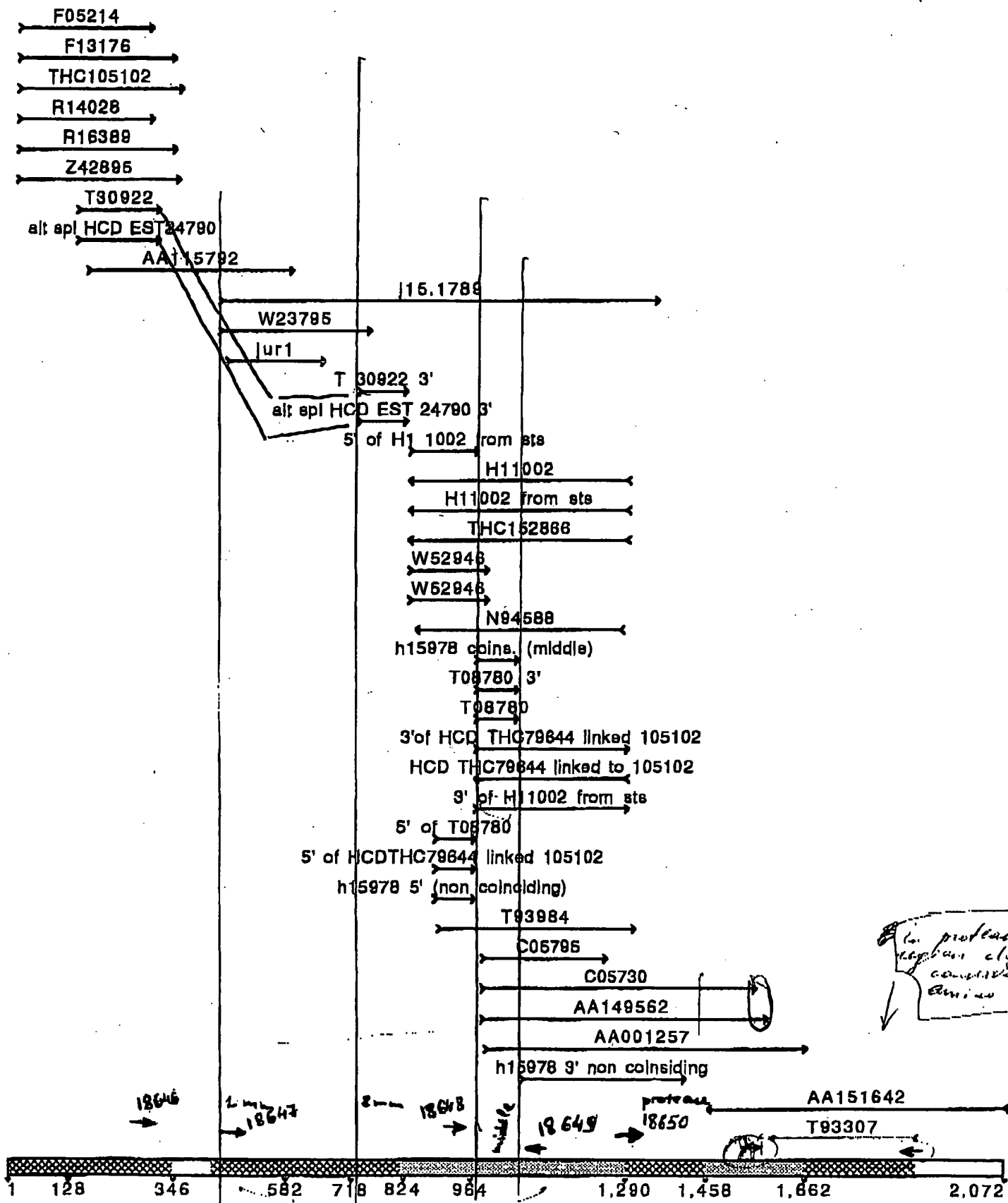
5' CAG TAC ACA GGC TCC AGA AGA AGT CAG CTT 3' 18651

yura

W.S.
0.4 1.1
0.25
0.25
0.25

Contig[0020]
Sequencher™ "big contig"

Exhibit L

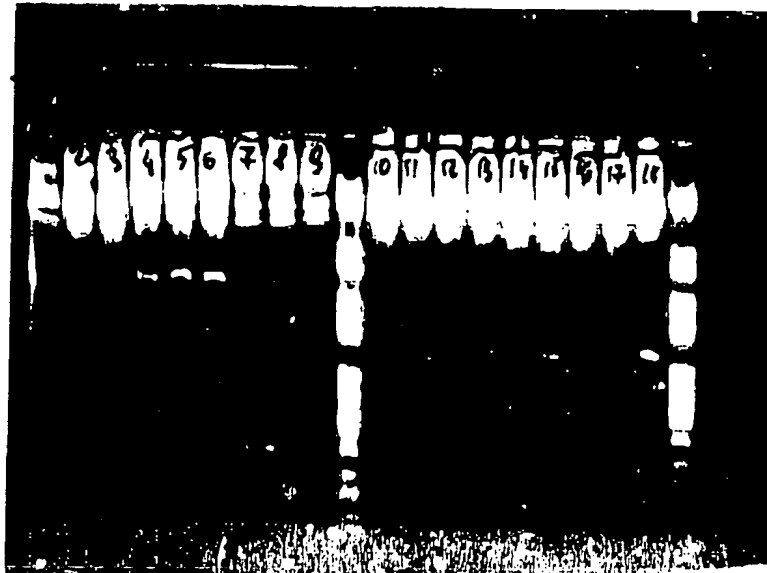


DATE _____

Sub 1 Sub 2
10000

111

Exhibit M



200
14
10
60

21

J



Vadim
clawer

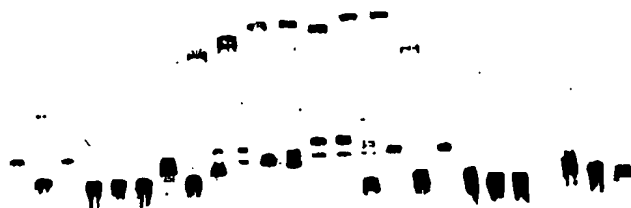
Galt

my PT 4 clawer

PT xho

112

DATE _____



1 2 3 4 5 6 7 8 9 10 11 12 13 14

BHI

RI

pcv1 [-> (XhoI/Sac)]

pcv2 (SalI/Sac)



1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

~~pcv1 (SalI/Sac)~~



1 2 3 4 5 6

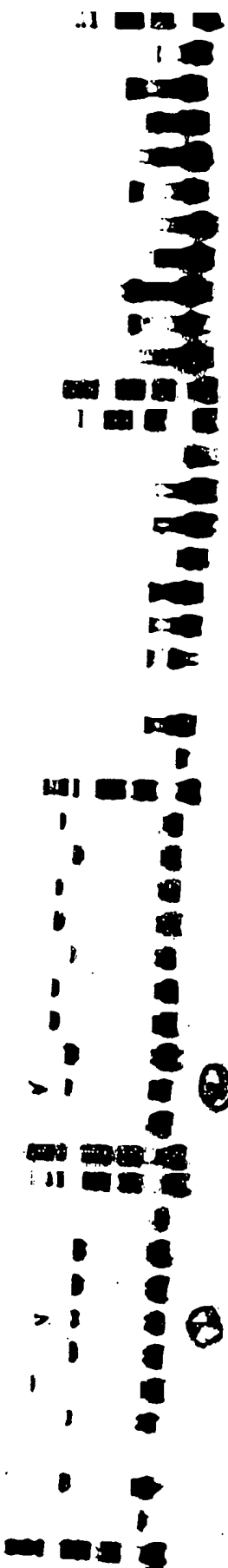
②③ pADH1 / RI

pGBS cont. / RI

④⑤ pGBS-t1 / RI

pAB ②③ / BHI

Delebia mutants v2



12/12/12

12/12/12

1

[Image]

[progress meter]

Search in progress, please wait for results

TBLASTN 1.4.9MP [26-March-1996] [Build 14:27:13 Apr 1 1996]

Reference: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol. 215:403-10.

Notice: statistical significance is estimated under the assumption that the equivalent of one complete reading frame of the database codes for protein and that significant alignments will involve only coding reading frames.

Query= tmpseq_1
(139 letters)

Database: Non-redundant Database of GenBank EST Division
824,500 sequences; 302,742,428 total letters.

Sequences producing High-scoring Segment Pairs:	Reading Frame	High Score	Smallest Sum Probability P(N)	N
gb AA198928 AA198928 mu23f09.r1 Soares 2NbMT Mus muscu...	+3	79	0.040	1
gb AA014850 AA014850 mh28c10.r1 Soares mouse placenta ...	+1	37	0.81	2
gb W23795 W23795 zb79a05.r1 Soares senescent fibro...	+3	63	0.9997	1

gb|AA198928|AA198928 mu23f09.r1 Soares 2NbMT Mus musculus cDNA clone
640265 5' similar to TR:G695247 G695247 ORF E8. ;
Length = 421

Plus Strand HSPs:

Score = 79 (36.9 bits), Expect = 0.040, P = 0.040
Identities = 25/106 (23%), Positives = 41/106 (38%), Frame = +3

Query: 5 EVLCEVARKLGTDDREVVLFLNLFIPQPTLAQLIGALRALKEEGRLTFPLLAECXXXXX 64
EV+ +V L D++E++LFL + L +L E G+L+F LAE
Sbjct: 99 EVIHQVEECLDEDEKEMMLFLCRDVTENLAAPNVRDLLDSLSERGQLSFATLAELLYRVR 278

Query: 65 XXXXXXXXXXXXXXXXXXXXERHLAGTMSYFSPYQLTVLHVDGELCARDI 110
E HL S Y++ ++ + L D+
Sbjct: 279 RFDLLKRILKTDKATVEDHLRRNPHLVSDYRVLLMEIGESLDQNDV 416

gb|AA014850|AA014850 mh28c10.r1 Soares mouse placenta 4NbMP13.5 14.5
Mus musculus cDNA clone 443826 5'
Length = 143

Plus Strand HSPs:

Score = 37 (17.3 bits), Expect = 1.7, Sum P(2) = 0.81
Identities = 9/14 (64%), Positives = 9/14 (64%), Frame = +1

Query: 87 TMSYFSPYQLTVLH 100
T S F P QLT V H
Sbjct: 19 TCSSF*PSQLTVKH 60

Score = 35 (16.3 bits), Expect = 1.7, Sum P(2) = 0.81
Identities = 5/6 (83%), Positives = 6/6 (100%), Frame = +3

Query: 134 CTVWKT 139
CTVW+T
Sbjct: 63 CTVWQT 80

gb|W23795|W23795 zb79a05.r1 Soares senescent fibroblasts NbHSF Homo
sapiens cDNA clone 309776 5'
Length = 313

Plus Strand HSPs:

Score = 63 (29.4 bits), Expect = 8.2, P = 1.0
Identities = 18/54 (33%), Positives = 28/54 (51%), Frame = +3

Query: 5 EVLCEVARKLGTDREVVLFLLNVFIPQPTLAQLIGALRALKEEGRLTFPLLA 58
EV+ +V L TD++E++LFL + L L+E G+L+ LAE
Sbjct: 18 EVIHQVEEALDTDEKEMLLFLCRDVAIDVVPNVRDLLDILRERGKLSVGDLAE 179

Parameters:

V=100
B=50
H=0
-filter=SEG
P=4

-ctxfactor=6.00
E=10

Query	Frame	MatID	Matrix name	----- Lambda	As Used K	----- H	----- Lambda	Computed K	----- H
+0	0	BLOSUM62	0.323	0.138	0.404	same	same	same	

Query	Frame	MatID	Length	Eff.Length	E	S	W	T	X	E2	S2
+0	0		139	118	10.	60	3	14	22	0.058	34

Statistics:

Query	Frame	MatID	Expected High Score	Observed High Score	HSPs Reportable	HSPs Reported
+0	0		63 (29.4 bits)	79 (36.9 bits)	4	4

Query	Neighborhd	Word	Excluded	Failed	Successful	Overlaps
Frame	MatID	Words	Hits	Extensions	Extensions	Excluded
+0	0	489	27788736	3256934	24493093	38709
						8

Database: Non-redundant Database of GenBank EST Division

Release date: February 16, 1997

Posted date: 7:38 AM EST Feb 16, 1997

of letters in database: 302,742,428

of sequences in database: 824,500

of database sequences satisfying E: 3

No. of states in DFA: 289 (31 KB)

Total size of DFA: 37 KB (64 KB)

Time to generate neighborhood: 0.00u 0.00s 0.00t Real: 00:00:00

No. of processors used: 4

Time to search database: 86.35u 0.35s 86.70t Real: 00:00:22

Total cpu time: 86.37u 0.39s 86.76t Real: 00:00:22

your ID: 10609.1818 ** our Ref: SampleB-1818 16
10609.1818.seq Length: 1021 February 25, 1997 21:08 Type: N Check: 5641 ..

```
1  ACCAAACCAA AAAAAGAGNC CTAGAACTAG TCGGAATTCG GCACGAGGTG
51  TCTGCTGAAG TCATCCATCA GGTGAAGAA GCACTTGATA CAGATGAGAA
101 GGAGATGCTG CTCTTTTGT GCCGGGATGT TGCTATAGAT GTGGTTCCAC
151 CTAATGTCAG GGACCTTCTG GATATTTTAC GGGAAAGAGG TAAGCTGTCT
201 GTCGGGGACT TGGCTGAACT GCTCTACAGA GTGAGGCGAT TTGACCTGCT
251 CAAACGTATC TTGAAGATGG ACAGAAAAGC TGTGGAGACC CACCTGCTCA
301 GGAACCCCTCA CCTTGTTTCG GACTATAGAG TGCTGATGGC AGAGATTGGT
351 GAGGATTGG ATAAATCTGA TGTGTCCTCA TTAATTTTCC TCATGAAGGA
401 TTACATGGGC CGAGGCAAGA TAAGCAAGGA GAAGAGTTTC TTGGACCTTG
451 TGGTTGAGTT GGAGAACTA AATCTGGTTG CCCCAGATCA ACTGGGATTT
501 ATTAGAAAAA ATGCCTAAAG AACATCCACA GAATAgACCT GAAGACAAAA
551 ATCCAGAAAGT ACAAGCAGTC TGTTCAGGA GCAGGGACAA GTTACAGGGA
601 ATGTTCTCCA AGCAGCAATC CAAAAGATCT CAAGGATCCT TCAAATAACT
651 TCAGGATGAT AACACCCTAT GCCCATTGTC CTGATCTGAA AATTCTTGGA
701 AATTGTTCCa TGTGATTAAC ATGGAAGTGC CTCTACTTAA TCNTCTGAAT
751 GATAAATCGT TCNTTTTCTA AATGTNTTAT AATGTNTTTA NCCCTTNCTT
801 GTTGCGGTAT TTAAATGCT TCCCATCTTT TGTTACTACT AATATGCNAT
851 AAATAAATTC CTTGTNCTCT TAAAAA AAAA AAAAANTTCC
901 CGCGCCCCCA CNCANGGGG GCCGGTCCCN TCCNNNTN ANTTTTTANT
951 CCNGGCCCTT TNCCCCTNNT GGGAACCCNT CTTNATCTNA ANGAAACCCC
1001 CNTCTNCNT GCCNCCCCC C
```

your ID: 11717.1818 ** our Ref: SampleB-1818 17
11717.1818.seq Length: 1028 February 25, 1997 21:08 Type: N Check: 5259 ..

```
1  CgATTcATAg ATCAGGGTTT TCCCAGTCAC GACGTTGTAA AACGACGGCC
51  AGTGAATTGT AATACgACTC ACTATAGGGC GAATTGGGTA CCGGGCCCCC
101 CCTCGAGGTC GAGCGGCCGC AGGAATTTTT TTTTTTTTTT TTTTTTTTTT
151 TTTTTTTTAA AAAGtACAAG GATATTTATT TTATAgCATT ATTAgtAgTA
201 ACAAAAAATT GGAAAgCATC TAAACATACA GCAACAANAA AGGGCTAAAC
251 ACaTTATAAC ACaTTTAgAA AATGAAACAA TTTAATCATT CAAAATGATT
301 AATTAAAGGC AgTtCCATNT TAATCACATG GAACAATTC CAAAATTTT
351 CAAATCAGGA CAATGGGCAT AGGGTGTTAT CATCCTGAAT TTATTTGAAG
401 GATCCTTGAA ACTCTTTTGG ATTGCTGCTT GGAAAACATt CCTGTAACCT
451 GTCCCTGCTC CTTGAACAAA CTGCTTGTA CTTCTGGATT TTGTCTtCAG
501 GTCTATTCTG TGGATgTTCT TTAGGCATTT TTCTAATAAA TCCAgTTGAT
551 CTGGGGCAAC CAAATTTATT TTCTCCAAC CAACCACAAG GTCCAAAAAA
601 CTCTTCTCCT TGCTTATCTT GCCTCGGCCC ATGTTTCCTT CaTGAGGAAA
651 ATTAATGAGG ACCTTCANAT TTATCCAANT CCTCNCCAAT CTCTGCCATC
701 AACTCTATA TTCCAAAACA AGGTGANGGT CCTGAACANG TGGGTCTCAC
751 ACTTTTCTGT CCNCTCCAA TANTTTGAAC AGGTCAAATC CCTCNTCTGT
801 TAAACATTCA CCANTTCCCN ACAAAAACTT ACCCTTTCCN TAAAATATCA
851 AAGGTCCTGA CTTANGTGAA CCCCTCTATA CCNCTCCCGC CCAAAAAAAC
901 CACCCCTCCC NNCTTTCATT CTCTCCCCCG AAGGAAAATC NCAAACCNCT
951 CCAATCCANT ATCCAGATCC TTTTNGGGT GGGGGGTCTC CCCCCAANAA
1001 NTTANNNCCC NCCTNTTGT TTANCCCC
```

your ID: 18648.1818 ** our Ref: SampleB-1818 18
18648.1818.seq Length: 1012 February 25, 1997 21:08 Type: N Check: 1701 ..

```
1  AANANGCcTA AAGAAcAtCC ACAGAATAGA CCTGAAGACA AAAATCCAgA
51 AGTACAAgCA GTCTGTTCAA GGAGCAGGGA CAAgTTACAG GAATGTTCTC
101 CAAGCAGCAA TCCAAAAGAG TCTCAAGGAT CCTTCAAATA ACTTCAGGAT
151 GATAACACCC TATGCCCATT GTCCTGATCT GAAAATTCTT GGAAATTGTT
201 CCATGTGATT AACATGGAAC TGCCTCTACT TAATCATTCT GAATGATTAA
251 ATCGTTTCAT TTTCTAAATG TGTATAATG TGTTTAGCCC TTTCTTGTTG
301 CTGTATGTTT AgATGCTTTC CAATCTTTTG TTACTACTAA TAATGCTATA
351 AAATAAATAT CCTTGTA CTTAAAAAAA AAAAAAAAAA aAAAAAAAAA
401 AAAAATTNCC TGCGGCCGCN CAACCTCAAG GGGGGGCCCC GTACCCAATN
451 CGCCCTATAN TNATTCTTAT TACAATNCAC TGGCCGNCGT TTTACAACNT
501 CGTNACTGGG AAAAACCCTN ATCTATNAAT CNTAAATACT GAAAAACCCC
551 GCAATTTTAC TTCAACTGTG CATCGTGCAC CGTCTCAATT TCTTTCNTTT
601 ATACNTCGTT TNGCCTTCTN TTATNTAACT ATACCCCCCN AANTTCCAAT
651 CTNGGCCNTG TANCCTCTGA TCTATAAAAA TTTTAAATG ACTAAAATAA
701 NTGCCCCCTT TTTTTTGGAC CTNCTTCTCN TGAANTTTNT NACAAAGGCT
751 ATCCAAANCT TGGACTCTNC CCNAAGTTGG TCAATCNCNA ACAGGTGTCG
801 GNTNTCTACC TTNCCAAAAA TTCCAAAAA AGNAAAGGTC AANCTTG GTA
851 ANCTTNTTAA ACTCCAATAC CAATCCTNNN ANTATNATNN TATNATNAAT
901 NATTTAAAAA ANNATNTTAN AATTAAATT GACCTAGGTT AAACAAAATT
951 CAANCCAATA CCNCCGTAGT CNGTCCTNCN GGTAACATAA NCCCTTGACC
1001 CCCCACGGCC CC
```

your ID: rti-651.1831 ** our Ref: SampleC-1831 20
rti-651.1831.seq Length: 765 March 3, 1997 11:26 Type: N Check: 1445 ..

```
1  CTCCGGTGAA CTGTGCACAG CCCTCGCTTC TGAGCCTTGA ATTCCACATT
51  CTTCATCGCT GGCCCATCCA CCTCCAAgAG GCTGCTGTTC TCCAGCTGGC
101 CCTCTGACAC CACATAGTTC TGAATAAAAA ACaTCTTTGG CTTCCCTGCT
151 AGATAAGGGC ATGAATCTCC CATGAACATC CTCCTGATGT GATGCAGGGG
201 GAGCCCTGAg TGAGTCTGAT CCACACCATA CACACTCTGG GAGCCTCCTC
251 GGCTCACCAG GACACACACa AAGCTGTCGT AGTCTCGGTG CTCGGGCATA
301 CAGGCAAATT GGCCAAGAAT CTGGGATATA CCATGCATAC TGAGATGCAA
351 GAATTTCTGG ACTTCATAGC CCAGGGGAAG TGAAGGTGTC TCGAAgAAGC
401 TCTGTCTCAT TGCCAATGCA ATCGATTATC AGGCAGATTC CTAGGGGCTT
451 GCTCTTCATC TTGTATCTCT CTTCAGGTAT GCTCTGAGGC AAAAAAGCTT
501 CTGATTCCtG AATGGATTTC TTTACTGGTT CTTGTtGAGC GCCAAGCTGT
551 TCCTTAAGTC TTTGTTCTTT ACTTCTCCCA TTATGGAGCC TGAAGTTATT
601 TgAAGGATCC TTGAgACtCT TTTGGATTGC TGCTTGAAA ACATTCCTGT
651 AACTTGTCCT TGCTCCTTGA ACAGATGCTT GTAtTCTNNG ANTTTTGTCT
701 CAGGTCTANT CTGTGGATGT CTTTAGGCAT TTTCTCATAA ATCCACTTGA
751 TTTGGGCACA AATTT
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your ID: rtl-648.1831 ** our Ref: SampleC-1831 19
rtl-648.1831.seq Length: 763 March 3, 1997 11:26 Type: N Check: 6251 ...

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151 TCCATAATGG GAGAAGTAAA GAACAAAGAC TTAAGGAACA GCTTGGCGCT
201 CAACAAGAAC CAGTGAAGAA ATCCATTCAG GAATCAGAAG CTTTTTTGCC
251 TCAGAGCATA CCTGAAGAGA GATACAAGAT GAAGAGCAAG CCCCTAGGAA
301 TCTGCCTGAT AATCGATTGC ATTGGCAATG AGACAGAGCT TCTTCGAGAC
351 ACCTTCACTT CCCTGGGCTA TGAAGTCCAg AAATTCTTGC ATCTCAGTAT
401 GCATGGTATA TCCCAGATTC TTGGCCAATT TGCCTGTATG CCCGAGCACC
451 GAGACTACgA CAGCTTTGTG TGTGTCCTGG TGAGCCGAGG AGGCTCCCAg
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551 CAGGAGGATG TTCATGGGAG ATTCATGCCC TTATCTAGCA GGGAAGCCAA
601 AGATGTTTTT TATTCAGAAC TATGTGGTGT CAGAAGGCCA gCTGGAgAAC
651 AgCACCTCTT GGAGGTGGAT GGCCACCANN AAAATGTGGA ATTCCAGGCT
701 CACAACCAAG GCTGTTGCCA TTTCACGACA AACTGANTTC CTCTGGAACC
751 TGTGTANGCG GGA
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Exhibit Q

your ID: v1-t7.1822 ** our Ref: SampleB-1822 23

v1-t7.1822.seq Length: 775 February 25, 1997 21:05 Type: N Check: 6815 ..

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201 TTTAgAAAAT GAAACgATTT AATCATTCAA AATGATTAAg TAAAGGCAGT
251 TCCATGTAA TCaCATGGAA CAATTTCCAA AAATTTTCag ATCAGGACAA
301 TGGGCATAGG GTGTTATCAT CCTGAAgTTA TTTGAAGGAT CCTTGAAACT
351 CTTTTGGATT GCTGCTTGGA AAACATTCCT GTAACCTGTC CCTGCTCCTT
401 GAACAAACTG CTTGTACTTC TGGATTTTTG TCTTCAGGTC TATTCTGTGG
451 ATGTTCTTTA GGCATTTTTC TAATAAATCC AGTTGATCTG GGGCAACCAA
501 ATTTAgTTTC TCCAACgCAA CCACAAGGTC CAAgAAACTC TTCTCCTTgC
551 TTATCTTGCC TCGGCCCATG TaATCCTTCN TGANGAAAAT TAATGAgGAC
601 CCTCCNATTT ATCCAAATCC TCCCAATCT CTGCCATCAN CACTCTATAN
651 TCCGAAACAA GGTGANGGTT CCTGAACAGG TGGGTCTCCC ANCTTTTCTG
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751 TCCACCAATT CCNANAAAAC TTAgCT
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your ID: vl.1822 ** our Ref: SampleB-1822 17
vl.1822.seq Length: 821 February 25, 1997 21:05 Type: N Check: 3460 ..

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1  GGANCGTCGA GGCATTACAA TCGCGAAACC AAGCCATAGC ATGAAACAGC
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251 GTTTCTTTGC CTCCATCTTG GGTGCGCCTT CCCGGCGTCT AgGGGAGCGA
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351 CCCaCTGGAA ACgATTCTGA AAGAAATgAA GTCAGCCCTC ATAAATGAAG
401 TTGACTGCCT GCTGGCTTTC TGTTGACTGG CCCGGAGCTG TACTGCaAGA
451 CCCTNGTGAG CTTCCCTAgT CTAAGAgTAN GATGTCTgCT GAAgTCaTCC
501 ATCAgGTTGA aCAagCCNTG ATNCCGATCA NANNGAGATC CTGCCCTTTC
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601 NTCTGGTATT TTTCACNGNN AACAGGTNCC TNTCTGTCCN GGAATNNGCT
651 NACTNCTCCA CTCAATNANG CGATNTNACC TGCTCNACTT CCTNCNATAT
701 GGACTNNCAT CCTGTGGAAN NCCTCTTNCT CATGACCCCT CTCCTTTTNC
751 CGTACTNACT ATTCNCCNGC TCAANATTNN TTAAGNNCTG NAANANTCNA
801 TCTTNTTCAT TATTTTTGCT C
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your ID: v2-t7.1822 ** our Ref: SampleB-1822 24

v2-t7.1822.seq Length: 820 February 25, 1997 21:05 Type: N Check: 4660 ..

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301 GTTTCTTATG TGTAGGAgAg GATAAGTTTC TTTCTCAGaA TGTGCTGCag
351 CCAGACATaA TATTTCTCCT TGGCAGAAAC TNTGCNGTTC CAATCATACA
401 TGTAGCCATT GCANTTCAAT GTGAANATCC ANGAAGTGGG CGTTTTCTTT
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801 AATTCATNAC CTTTTANTCC
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your ID: v4-t7.1822 ** our Ref: SampleB-1822 25

v4-t7.1822.seq Length: 797 February 25, 1997 21:05 Type: N Check: 6426 ..

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201 AANGGGNTAA ACNCNTTATA ACNCNTTTAA AAAATGAAAC AATTTAATCN
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401 TTCCTGTAAC TTGTCCCTGC NCCTTGAACA AACTGCTTGT NCTTCNGGAT
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551 AGGTCCAAAA AACTCTTCTC CTTGCTTATC TTGCCTCGGC CCATGTTATC
601 CTTCTGAGG AAAATTAATG AGGACCCTCN AATTTATCCA AATCCCCCCA
651 ATCTCTGCCA TCANCACTCT ATANTCCGGG TTTCCCNAAAT GGTAATGGCC
701 TCAAANGATC CNTATCNANA TGTCCCNAAA TNATCCGGCA AAAAAAACC
751 CGGGCGNTTC NGTCCCAACG AAANCAAAAT TCNAACGGAG GCGGACG
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your ID: v4.1822 ** our Ref: SampleB-1822 19
v4.1822.seq Length: 836 February 25, 1997 21:05 Type: N Check: 7807 ..

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151 TCTTGGACCT TGTGGTTGAG TTGGAGAAAC TAAATCTGGT TGCCCCACAT
201 CAACTGGATT TATTaGAaAA ATGCCTACAg AACATCCACA CAATNCACCT
251 GAAgACCaAA ATCCAGAAGT ACAAgCATTc TGTTCaAGGA GCAGGGACaA
301 GTTACCCGAA TGTTCCTCCNN TCANCNATCC AAAAGANTCT CANNGGATCC
351 TTCACATAAC TTCNCGATGA TNACACCCTA NGCCCNTTGT CCTGATCTGA
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501 TNTANCCCTC TCNTGTTGCC TGTATGTCTA CATNCTTTCC NNTCNTTCGT
551 TACTNCTANT AATGCTCTNN TATATNTATC CTTGTNCTTC TCTCTCTTCC
601 NCTCCCNCTT CTCNTCTCC TTTCTCCCT CCCNCCNTNC TCCCTTCTCT
651 TNCCTCTCTC TCNNNNCATT AAGGCNCCCC GCTACTTCAA NGGCCCCCAN
701 GGNCCCCNAC ANTNNTTCTT NTTTTTACCC TCCCCCTTNC CCCNNAAGTT
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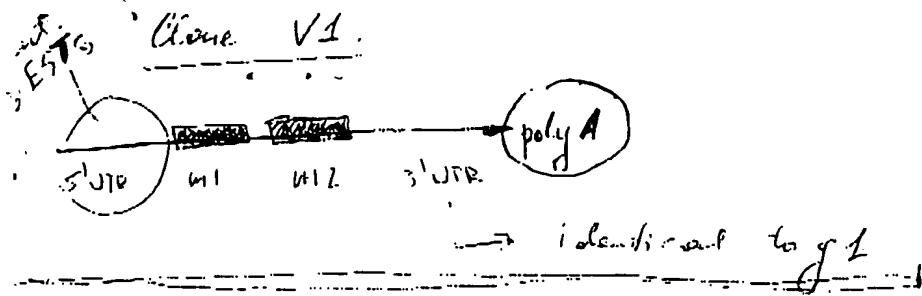
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151 GTTCCATGTT AATCACATGG AACAATTTCC AAAAATTTTC AgATCAGGAC
201 AATGGGCATA GGGTGTATC ATCCTGAAgT TATTTGAAGG ATCCTTGAAA
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351 GGATGTTCTT TAGGCATTTT TCTAATAAAT CCAgTTGATC TGGGGCAACC
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551 ATAATCCGAA ACAANGTGAA GGTCNTGAA CACGTGGGTC TCCACACCTT
601 TTCTGTCCTC TTCAAAATAC TTTGAACAGG TCAATCCCCa CTCTGTAAAC
651 ATTCACCCAG TCCCgACNAN NCTTACTCTT TCCNTAAATN CCNAANGTCC
701 NACTTAGTNG AACNCCCTTT NCTCCCCCGN CCAAAAANCC CCCTCNTCGT
751 TTAATNNTCN CCCCgangag ACNTCCANTC NNCTNACAGG NAC
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your ID: v6-t7.1822 ** our Ref: SampleB-1822 27

v6-t7.1822.seq Length: 779 February 25, 1997 21:05 Type: N Check: 1979 ..

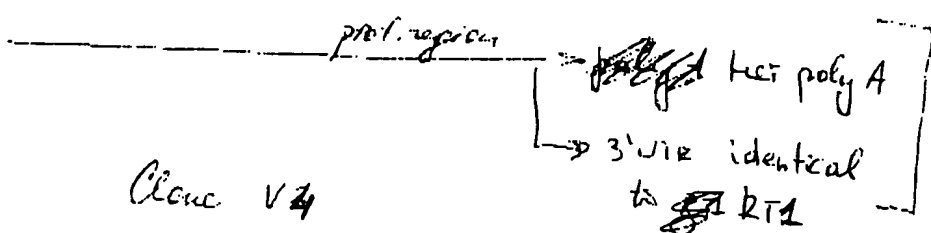
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151 AGTTCCATGT TAATCACATG GAACAATTTT CAAgAATTTT CAgATCAGGA
201 CAATGGGCAT AGGGTGTTAT CATCCTGAAG TTATTTGAAG GATCCTTGAg
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301 CTTGAACAgA CTGCTTGCTT TTCTGGATTT TTGTCTTCAG GTCTATTCTG
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401 CAgATTTAGT TTCTCCAAC CAACCACAAG GTCCAAGAAA ACTCTTCTCC
451 TTGCTTATCT TGCCTCGGCC CATGTTATCC TTCATGAGGA AAATTAATGA
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551 TATAgTCCGA AACAAGGTGA AGGTTCTCTGA ACAGGTGGGT CTCCACAGCT
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651 AAACATTCAC CATTTCCCGA CAAANNCTTA CTCTTTCCCG TNAAATACCN
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751 AACACNCCNC TTCTCTNNNT TCAATTTCT
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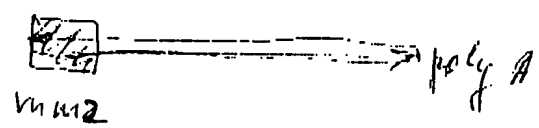
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Exhibit R

Clone V2



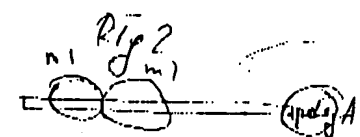
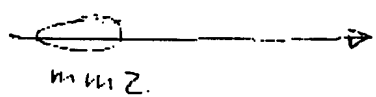
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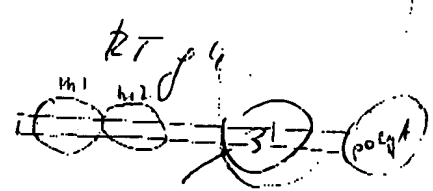
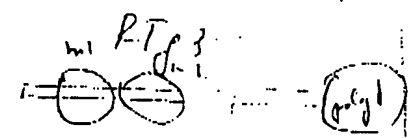
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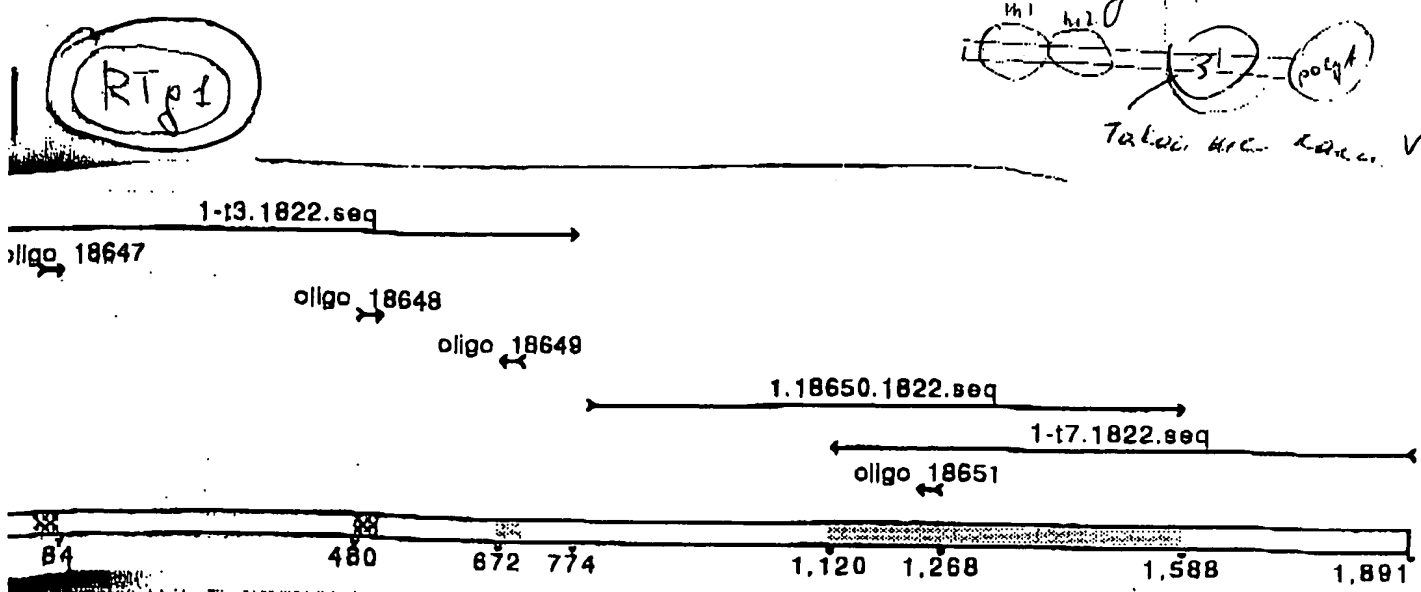
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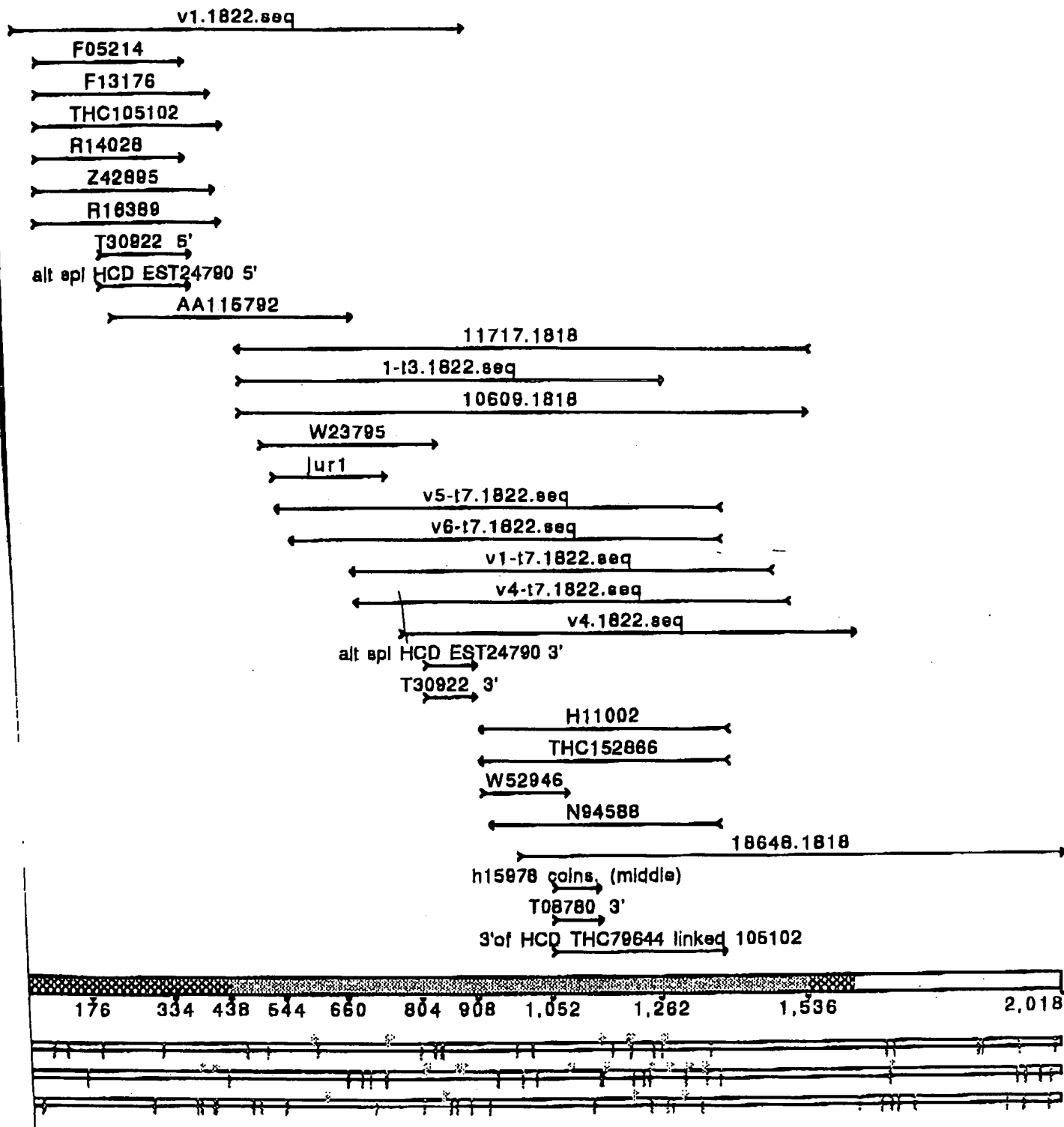
poly A 3'



Taken from RTg1



clone 1 non corr left part
Sequencher™ "temp oral"



Contig[0059]
Sequencher™ "temporal"

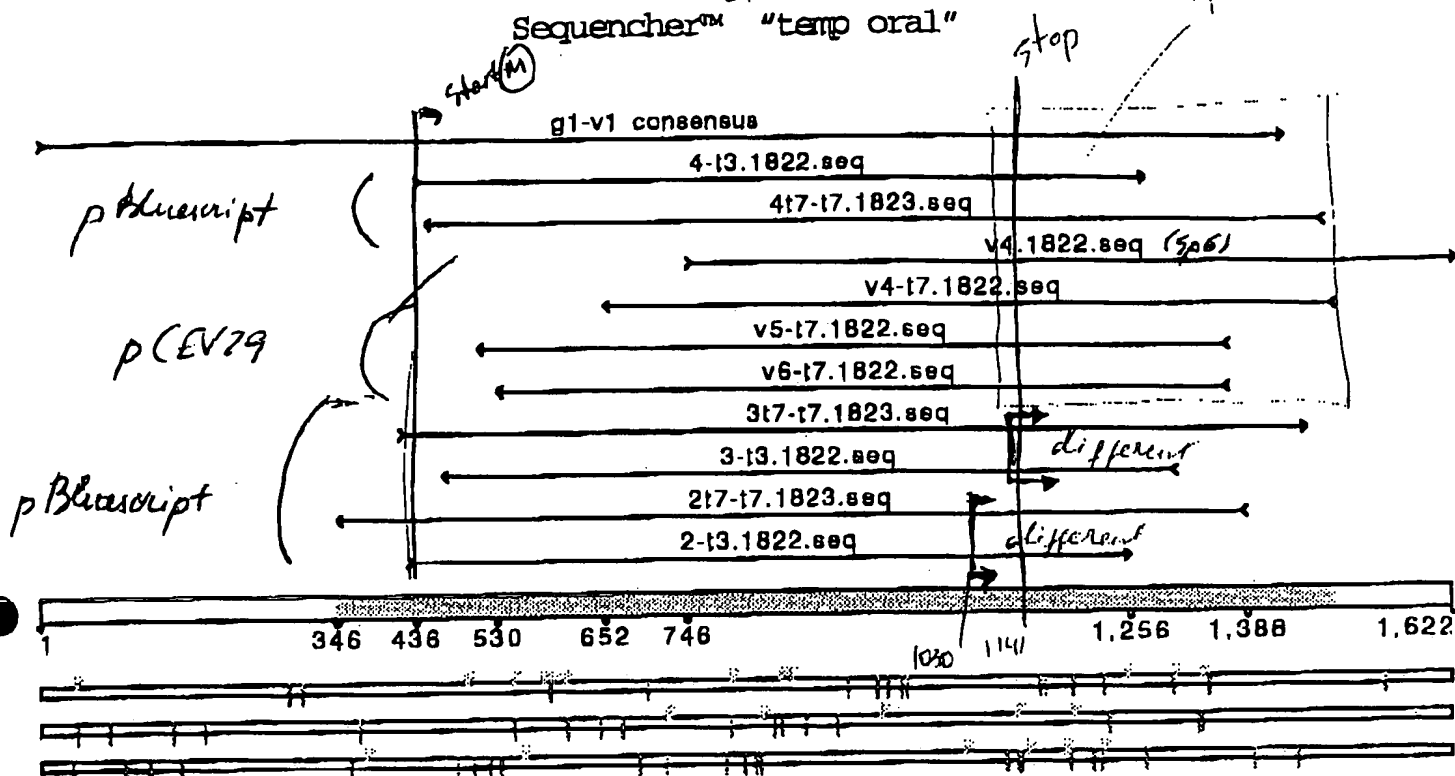


Diagram Key.	
	Hole in contig
	Single fragment
	Multiple fragments same direction
	Both strands
	Both strands plus
	Start codon frame 1
	Stop codon frame 2
	Bumps on fragments show motifs, hollow rectangles show features